EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	. 1	("0688802").PN.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2007/02/22 06:27
L2	2	("6888027").PN.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2007/02/22 06:27
L3	2	("6087367").PN.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2007/02/22 06:27
L4	2	("9816503").PN.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2007/02/22 06:27
L5	2	("5534654").PN.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2007/02/22 06:27
L6	1209	HDAC .	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/02/22 06:28
L7 .	2232	histone adj deacetylase	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/02/22 06:28
L8	2603	l6 or l7	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/02/22 06:29
L9	13476	hydroxam\$	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/02/22 06:29
L10	460	17 and 19	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/02/22 06:29
L11	302	17 same 19	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/02/22 06:31



EAST Search History

L12	10	"6541661"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/02/22 07:03
L13	10	"9816503"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/02/22 07:49
L14	6	"5534654"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/02/22 09:10
L15	266	562/623.ccls.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/02/22 09:10
L16	11	110 and 115	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/02/22 09:11

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         OCT 30
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         NOV 03
NEWS
                 JAPIO enhanced with IPC 8 features and functionality
         NOV 10
NEWS
                 CA/CAplus F-Term thesaurus enhanced
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         NOV 10
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         NOV 20
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         DEC 01
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         DEC 11
                 CAS REGISTRY chemical nomenclature enhanced
         DEC 14
NEWS 11
                 WPIDS/WPINDEX/WPIX manual codes updated
NEWS 12
        DEC . 14
                 GBFULL and FRFULL enhanced with IPC 8 features and
                 functionality
NEWS 13 DEC 18
                 CA/CAplus pre-1967 chemical substance index entries enhanced
                 with preparation role
NEWS 14 DEC 18
                 CA/CAplus patent kind codes updated
NEWS 15 DEC 18
                 MARPAT to CA/CAplus accession number crossover limit increased
                 to 50,000
NEWS 16 DEC 18
                 MEDLINE updated in preparation for 2007 reload
NEWS 17 DEC 27
                 CA/CAplus enhanced with more pre-1907 records
NEWS 18 JAN 08
                 CHEMLIST enhanced with New Zealand Inventory of Chemicals
NEWS 19 JAN 16
                 CA/CAplus Company Name Thesaurus enhanced and reloaded
NEWS 20 JAN 16 IPC version 2007.01 thesaurus available on STN
NEWS 21 JAN 16 WPIDS/WPINDEX/WPIX enhanced with IPC 8 reclassification data
NEWS 22 JAN 22
                 CA/CAplus updated with revised CAS roles
NEWS 23 JAN 22
                 CA/CAplus enhanced with patent applications from India
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                 CAS Registry Number crossover limit increased to 300,000 in
                 multiple databases
                 CASREACT coverage to be extended
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         FEB 13
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                 PATDPASPC enhanced with Drug Approval numbers
         Feb 15
NEWS 28
        Feb 15
                 RUSSIAPAT enhanced with pre-1994 records
              NOVEMBER 10 CURRENT WINDOWS VERSION IS V8.01c, CURRENT
NEWS EXPRESS
              MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
              AND CURRENT DISCOVER FILE IS DATED 25 SEPTEMBER 2006.
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              STN Operating Hours Plus Help Desk Availability
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              For general information regarding STN implementation of IPC 8
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chain nodes :

7 8 9 10 11 12 13 14 15 16 23 24

ring nodes :

1 2 3 4 5 6 17 18 19 20 21 22

chain bonds :

 $2-13 \quad 6-8 \quad 7-10 \quad 7-8 \quad 9-10 \quad 10-11 \quad 11-12 \quad 13-14 \quad 13-15 \quad 13-16 \quad 14-17 \quad 20-23 \quad 23-24$

ring bonds :

1-2 1-6 2-3 3-4 4-5 5-6 17-18 17-22 18-19 19-20 20-21 21-22

exact/norm bonds :

2-13 9-10 10-11 13-14 13-15 13-16 14-17 20-23 23-24

exact bonds :

6-8 7-10 7-8 11-12

normalized bonds :

1-2 1-6 2-3 3-4 4-5 5-6 17-18 17-22 18-19 19-20 20-21 21-22

Match level:

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:CLASS 10:CLASS 11:CLASS 12:CLASS 13:CLASS 14:CLASS 15:CLASS 16:CLASS 17:Atom 18:Atom 19:Atom 20:Atom 21:Atom 22:Atom 23:CLASS 24:CLASS

L1 STRUCTURE UPLOADED

=> d 11

L1 HAS NO ANSWERS

L1

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=> search l1 exact full
FULL SEARCH INITIATED 10:39:28 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 45 TO ITERATE

100.0% PROCESSED 45 ITERATIONS

2 ANSWERS

SEARCH TIME: 00.00.01

L2 2 SEA EXA FUL L1

=> \\d scan 8598666 D 47 SCAN L3 0 \\D SCAN (D(W)SCAN)

=> d scan 12

L2 2 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN

MF C16 H16 N2 O5 S

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1

L2 2 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN

MF C16 H16 N2 O5 S

Double bond geometry as shown.

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=> 12

L4 2 L2

=> d 14 1-2 ti fbib abs

- L4 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2007 ACS on STN
- TI Novel sulfonamide derivatives as inhibitors of histone deacetylase
- AN 2005:842556 CAPLUS
- DN 143:359422
- TI Novel sulfonamide derivatives as inhibitors of histone deacetylase
- AU Finn, Paul W.; Bandara, Morwena; Butcher, Chris; Finn, Angela; Hollinshead, Ruth; Khan, Nagma; Law, Norman; Murthy, Sreenivasa; Romero, Rosario; Watkins, Clare; Andrianov, Victor; Bokaldere, Rasma M.; Dikovska, Klara; Gailite, Vija; Loza, Einars; Piskunova, Irina; Starchenkov, Igor; Vorona, Maxim; Kalvinsh, Ivars
- CS TopoTarget UK Ltd., Abingdon, OX14 4RY, UK
- SO Helvetica Chimica Acta (2005), 88(7), 1630-1657

CODEN: HCACAV; ISSN: 0018-019X

- Verlag Helvetica Chimica Acta PB
- DT Journal LA English
- OS CASREACT 143:359422
- Inhibition of the enzyme histone deacetylase (HDAC) is emerging as a novel AΒ approach to the treatment of cancer. A series of novel sulfonamide derivs. were synthesized and evaluated for their ability to inhibit human HDAC. Compds. were identified which are potent enzyme inhibitors, with IC50 values in the low nanomolar range against enzyme obtained from HeLa cell exts., and with antiproliferative effects in cell culture. Extensive characterization of the structure-activity relationships of this series identified key requirements for activity. These include the direction of the sulfonamide bond and substitution patterns on the central Ph ring. The alkyl spacer between the aromatic head group and the sulfonamide functionality also influenced the HDAC inhibitory activity. One of these compds., mll.1, also designated PXD101, has entered clin. trials for solid tumors and haematol. malignancies.
- RE.CNT 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT
- ANSWER 2 OF 2 CAPLUS COPYRIGHT 2007 ACS on STN
- Preparation of aryl-substituted N-hydroxy amides with sulfonamide linkages as HDAC inhibitors for treatment of proliferative conditions
- 2002:293604 CAPLUS
- DN 136:325325
- Preparation of aryl-substituted N-hydroxy amides with sulfonamide linkages as HDAC inhibitors for treatment of proliferative conditions
- Watkins, Clare J.; Romero-Martin, Maria-Rosario; Moore, Kathryn G.; Ritchie, James; Finn, Paul W.; Kalvinsh, Ivars; Loza, Einars; Dikovska, Klara; Gailite, Vija; Vorona, Maxim; Piskunova, Irina; Starchenkov, Igor; Adrianov, Victor; Harris, C. John; Duffy, James E. S.
- PA Prolifix Limited, UK
- SO PCT Int. Appl., 267 pp. CODEN: PIXXD2
- DТ Patent
- LA English

| FAN. | .CNT 1 PATENT NO. | | | | | KIND DATE | | | | APP: | LICAT | DATE | | | | | | |
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A3 20020627 | | | | WO 2 | 2001- | | 20010927 | | | | |
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| EP | 1328 | | | | A2 | | | 0723 | E | ΞP | 2001- | 9700 | 11 | | 20010927 |
| | R: | ΑT, | BE, | CH, | DE, | DK, | ES, | FR, | GB, | GF | R, IT, | LI, | LU, | NL, S | SE, MC, PT, |
| | | ΙE, | SI, | LT, | LV, | FI, | RO, | MK, | CY, | ΑI | , TR | | | | |
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| JP | 2004 | 5114 | 62 | | T | : | 2004 | 0415 | | | 2002- | | | | 20010927 |
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| NZ | 52543 | 39 | | | Α | 2 | 2004 | 1126 | N | ΙZ | 2001- | 52543 | 39 | | 20010927 |
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| | 20040 | | 26 | | A1 | | 20040 | | U | S | 2003- | 38179 | 90 | | 20030820 |
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| US | 20051 | L0744 | 15 | | A1 | 2 | 20050 |)519 | | | 2004- | | _ | | 20040329 |
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| | | | | | | | | | | | 2000-2 | | | A | 20000929 |
| | | | | | | | | | U | S 2 | 2001-2 | 29778 | 14P | P | 20010614 |
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MARPAT 136:325325

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AB

The title compds. AQ1JQ2CONHOH (I) [wherein A = aryl group; Q1 = covalentbond or aryl leader group having a backbone of at least 2 C atoms; J =SO2NR1 or NR1SO2; R1 = sulfonamido substituent; Q2 = acid leader group; with the proviso that if J is SO2NR1, then Q1 is an aryl leader group; and pharmaceutically acceptable salts, solvates, amides, esters, ethers, chemical protected forms, and prodrugs thereof] were prepared as histone deacetylase (HDAC) inhibitors for treatment of proliferative conditions, such as cancer and psoriasis. For example, 3-(3-sulfonylphenyl)acrylic acid Me ester (preparation given) was coupled with 1-aminonaphthalene to give the sulfonamide (51%). Deesterification (79%), followed by conversion to the acid chloride (99%) and treatment with HONH2.HCl in the presence of NaHCO3 in THF, afforded N-hydroxy-3-[3-(naphthalen-1ylsulfamoyl)phenyl]acrylamide (PX117228) in 24% yield. The latter inhibited HDAC from crude human cervical adenocarcinoma (HeLa) extract with IC50 of 7 nM and inhibited cell proliferation against the HeLa cell line using cell proliferation reagent WST-1 with IC50 of 0.8 nM.

Structure-activity relationship studies showed superior activity for I when (1) a reverse sulfonamide, i.e. NHSO2, was employed as J, (2) a covalent bond or aryl leader having a backbone of at least 2C atoms was used as Q1, and/or (3) a phenylene-meta-alkylene linkage was employed as Q2.

=> logoff hold COST IN U.S. DOLLARS TOTAL SINCE FILE ENTRY SESSION FULL ESTIMATED COST 11.77 81.48 DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE TOTAL ENTRY SESSION CA SUBSCRIBER PRICE -1.56-1.56

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=>

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chain nodes :

7 8 9 10 11 12 13 14 15

ring nodes :

1 2 3 4 5 6

chain bonds :

6-7 7-9 8-9 9-10 10-11 12-14 12-13 13-15

ring bonds :

1-2 1-6 2-3 3-4 4-5 5-6

exact/norm bonds :

8-9 9-10 12-14 12-13 13-15

exact bonds :

6-7 7-9 10-11

normalized bonds :

1-2 1-6 2-3 3-4 4-5 5-6

Match level:

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:CLASS 10:CLASS 11:CLASS 12:CLASS 13:CLASS 14:CLASS 15:Atom 16:Atom

L5 STRUCTURE UPLOADED

=> d 125

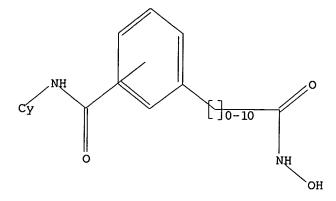
L25 NOT FOUND

The L-number entered has not been defined in this session, or it has been deleted. To see the L-numbers currently defined in this session, enter DISPLAY HISTORY at an arrow prompt (=>).

=> d 15

L5 HAS NO ANSWERS

L5 STR



Structure attributes must be viewed using STN Express query preparation.

=> search 15 sss sam

SAMPLE SEARCH INITIATED 11:24:53 FILE 'REGISTRY'

SAMPLE SCREEN SEARCH COMPLETED -1227 TO ITERATE

100.0% PROCESSED 1227 ITERATIONS

0 ANSWERS

29 ANSWERS

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**

BATCH **COMPLETE**

PROJECTED ITERATIONS: 22439 TO 26641 0

PROJECTED ANSWERS: 0 TO

L6 O SEA SSS SAM L5

=> search 15 sss full

FULL SEARCH INITIATED 11:25:05 FILE 'REGISTRY'

FULL SCREEN SEARCH COMPLETED - 24958 TO ITERATE

100.0% PROCESSED 24958 ITERATIONS

SEARCH TIME: 00.00.01

L7 29 SEA SSS FUL L5

=> d scan

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1,2-Benzenedicarboxamide, N-[8-(dimethylamino)-1-naphthalenyl]-N'-hydroxy-(9CI)

MF C20 H19 N3 O3

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):29

L7 29 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN

IN 1,2-Benzenedicarboxamide, N-hydroxy-N'-(2-nitro-3-pyridinyl)- (9CI)

MF C13 H10 N4 O5

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L7 29 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN

IN 1,2-Benzenedicarboxamide, N-hydroxy-N'-(2-mercaptophenyl)- (9CI)

MF C14 H12 N2 O3 S

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L7 29 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN

IN 1,2-Benzenedicarboxamide, N-hydroxy-N'-(2-hydroxyphenyl)- (9CI)

L7 29 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN

IN 1,2-Benzenedicarboxamide, N-hydroxy-N'-(2-hydroxy-4-nitrophenyl)- (9CI)

MF C14 H11 N3 O6

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L7 29 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN

IN 1,4-Benzenedicarboxamide, N-hydroxy-N'-(5,6,7,8-tetrahydro-5,5,8,8-tetramethyl-2-naphthalenyl)- (9CI)

MF C22 H26 N2 O3

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L7 29 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN

IN 1,4-Benzenedicarboxamide, N-(3,4-dimethylphenyl)-N'-hydroxy- (9CI)

MF C16 H16 N2 O3

L7 29 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN

IN 1,4-Benzenedicarboxamide, N-(4-butylphenyl)-N'-hydroxy- (9CI)

MF C18 H20 N2 O3

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L7 29 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN

IN 1,4-Benzenedicarboxamide, N-hydroxy-N'-(4-propylphenyl)- (9CI)

MF C17 H18 N2 O3

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L7 29 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN

IN 1,4-Benzenedicarboxamide, N-hydroxy-N'-(3-methylphenyl)- (9CI)

MF C15 H14 N2 O3

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L7 29 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN

IN 1,4-Benzenedicarboxamide, N-(2,3-dihydro-1H-inden-1-yl)-N'-hydroxy- (9CI)

MF C17 H16 N2 O3

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L7 29 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN

IN 1,4-Benzenedicarboxamide, N-cyclohexyl-N'-hydroxy- (9CI)

MF C14 H18 N2 O3

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L7 29 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN

IN Benzamide, 3-[3-(hydroxyamino)-3-oxo-1-propenyl]-N-phenyl- (9CI)

MF C16 H14 N2 O3

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L7 29 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN

IN 1,2-Benzenedicarboxamide, N-hydroxy-N'-phenyl- (9CI)

MF C14 H12 N2 O3

L7 29 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN

1,4-Benzenedicarboxamide, 2-chloro-N1-[4-chloro-3-(2-pyridinyl)phenyl]-N4-IN hydroxy- (9CI) C19 H13 C12 N3 O3

MF

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L7 29 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN

1,2-Benzenedicarboxamide, N-(2-aminophenyl)-N'-hydroxy- (9CI) IN

MF C14 H13 N3 O3

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L7 29 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN

IN 1,2-Benzenedicarboxamide, N-(3-acetylphenyl)-N'-hydroxy- (9CI)

MF C16 H14 N2 O4

L7 29 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN

IN 1,2-Benzenedicarboxamide, N-hydroxy-N'-(3-hydroxy-2-naphthalenyl)- (9CI)

MF C18 H14 N2 O4

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L7 29 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN

IN 1,2-Benzenedicarboxamide, N-hydroxy-N'-(2-hydroxy-3-methylphenyl)- (9CI)

MF C15 H14 N2 O4

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L7 29 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN

IN 1,2-Benzenedicarboxamide, N-hydroxy-N'-(2-hydroxy-5-methylphenyl)- (9CI)

MF C15 H14 N2 O4

L7 29 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN

IN 1,4-Benzenedicarboxamide, N-hydroxy-N'-tricyclo[3.3.1.13,7]dec-1-yl- (9CI)

MF C18 H22 N2 O3

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L7 29 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN

IN 1,4-Benzenedicarboxamide, N-[4-(1,1-dimethylethyl)phenyl]-N'-hydroxy(9CI)

MF C18 H20 N2 O3

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L7 29 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN

IN 1,4-Benzenedicarboxamide, N-hydroxy-N'-[4-(1-methylethyl)phenyl]- (9CI)

MF C17 H18 N2 O3

L7 29 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN

IN 1,4-Benzenedicarboxamide, N-(4-ethylphenyl)-N'-hydroxy- (9CI)

MF C16 H16 N2 O3

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L7 29 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN

IN 1,4-Benzenedicarboxamide, N-hydroxy-N'-(4-methylphenyl)- (9CI)

MF C15 H14 N2 O3

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L7 29 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN

IN 1,4-Benzenedicarboxamide, N-cyclopropyl-N'-hydroxy- (9CI)

MF C11 H12 N2 O3

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L7 29 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN

IN Benzenehexanamide, N, &-dihydroxy-4-[(phenylamino)carbonyl]-,

(ɛR)- (9CI) C19 H22 N2 O4

MF

Absolute stereochemistry.

PhNH
$$OH$$
 $CH_2)$ 4 N H OH

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L7 29 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN

IN Benzenepropanamide, 4-[[(2-aminophenyl)amino]carbonyl]-N-hydroxy- (9CI)

MF C16 H17 N3 03

HO-NH-C-CH₂-CH₂

$$0$$
 H_2 N
 C -NH

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L7 29 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN

IN 1,4-Benzenedicarboxamide, N-hydroxy-N'-phenyl- (9CI)

MF C14 H12 N2 O3

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

ALL ANSWERS HAVE BEEN SCANNED

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FULL ESTIMATED COST

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=> 17

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- 1. Begin with a letter,
- 2. Have 1-12 characters,
- 3. Contain only letters (A-Z) and numbers (0-9),
- 4. End with /Q for a query (search profile, structure, or screen set), /A for an answer set, or /L for an L-number list.
- 5. Not already be in use as a saved name,
- 6. Not be END, SAV, SAVE, SAVED
- 7. Not have the form of an L-number (Lnnn). ENTER NAME OR (END):ends/a ANSWER SET L8 HAS BEEN SAVED AS 'ENDS/A'

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1.8 ANSWER 1 OF 12 CAPLUS COPYRIGHT 2007 ACS on STN

Preparation of arylpyridines as inhibitors of hedgehog signalling.

- L8 ANSWER 2 OF 12 CAPLUS COPYRIGHT 2007 ACS on STN
- TI Compounds for inhibiting copper-containing amine oxidases and their use in inflammatory disease
- L8 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2007 ACS on STN
- TI Preparation of tetrahydronaphthalene hydroxamates and benzamides as histone deacetylase (HDAC) inhibitors.
- L8 ANSWER 4 OF 12 CAPLUS COPYRIGHT 2007 ACS on STN
- TI Preparation of arylhydroxamates as elastase and collagenase expression inhibitors for preventing skin aging.
- L8 ANSWER 5 OF 12 CAPLUS COPYRIGHT 2007 ACS on STN
- TI Preparation of thiophenedicarboxamides and related compounds as histone deacetylase (HDAC) inhibitors.
- L8 ANSWER 6 OF 12 CAPLUS COPYRIGHT 2007 ACS on STN
- TI Preparation of N-acylaminoalkanehydroxamic acids as IL-6 production inhibitors
- L8 ANSWER 7 OF 12 CAPLUS COPYRIGHT 2007 ACS on STN
- TI Preparation of alkanoic acid derivatives as novel class of cytodifferentiating agents and histone deacetylase inhibitors, and methods of use thereof
- L8 ANSWER 8 OF 12 CAPLUS COPYRIGHT 2007 ACS on STN
- TI Preparation of hydroxamic acids and their use as antitumor agents
- L8 ANSWER 9 OF 12 CAPLUS COPYRIGHT 2007 ACS on STN
- TI Preparation of arylhydroxamates and related compounds as potent inducers of terminal differentiation.
- L8 ANSWER 10 OF 12 CAPLUS COPYRIGHT 2007 ACS on STN
- TI Preparation of alkanedicarboxylic acid amides as novel potent inducers of terminal differentiation of neoplastic cell
- L8 ANSWER 11 OF 12 CAPLUS COPYRIGHT 2007 ACS on STN
- TI Nucleophilic reactions of N-hydroxy-, methoxy-, 2,3-epoxypropoxy-phthalimides
- L8 ANSWER 12 OF 12 CAPLUS COPYRIGHT 2007 ACS on STN
- TI Alkanedioic acid derivatives, novel potent inducers of terminal differentiation and methods of use thereof

=> d 18 1-12 ti fbib abs it

- L8 ANSWER 1 OF 12 CAPLUS COPYRIGHT 2007 ACS on STN
- TI Preparation of arylpyridines as inhibitors of hedgehog signalling.
- AN 2006:238237 CAPLUS
- DN 144:311912
- TI Preparation of arylpyridines as inhibitors of hedgehog signalling.
- IN Gunzner, Janet; Sutherlin, Daniel; Stanley, Mark; Bao, Liang; Castanedo, Georgette; Lalonde, Rebecca; Wang, Shumei; Reynolds, Mark; Savage, Scott; Malesky, Kimberly; Dina, Michael
- PA Genentech, Inc., USA; Curis Incorporation
- SO PCT Int. Appl., 256 pp. CODEN: PIXXD2
- DT Patent
- LA English
- FAN.CNT 1

PATENT NO. KIND DATE APPLICATION NO. DATE

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WO 2006028958
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OS MARPAT 144:311912 GI

Title compds. [I; A = carbocyclyl, heterocyclyl; X = alkylene, NR4CO, NR4CS, NR4SO2, NR4PO(OH), etc.; R1 = (substituted) alkyl, carbocyclyl, heterocyclyl; R2 = halo, OH, (substituted) alkyl, acyl, alkoxy; R3 = halo, OH, CO2H, (substituted) alkyl, acyl, alkoxy, alkoxycarbonyl, carbamoyl, alkylthio, sulfinyl, sulfonyl, carbocyclyl, heterocyclyl; R4 = H, alkyl; m, n = 0-3], were prepared for treatment of cancer (no data). Thus, N-[4-chloro-3-(pyridin-2-yl)phenyl]-6-chloro-3-carboxamide and 2-morpholinoethylamine were heated in BuOH in a sealed tube to give 6-(2-morpholinoethylamino)-N-[4-chloro-3-(pyridin-2-yl)phenyl]-6-chloro-3-carboxamide.

IT Pancreas, neoplasm

(adenocarcinoma; preparation of arylpyridines as inhibitors of hedgehog signaling)

IT Skin, neoplasm

(basal cell carcinoma, treatment; preparation of arylpyridines as inhibitors of hedgehog signaling)

IT Carcinoma

(basal cell, treatment; preparation of arylpyridines as inhibitors of hedgehog signaling)

IT Mammary gland, neoplasm

(carcinoma, treatment; preparation of arylpyridines as inhibitors of hedgehog signaling)

IT Carcinoma

(mammary, treatment; preparation of arylpyridines as inhibitors of hedgehog signaling)

IT Brain, neoplasm

(medulloblastoma, treatment; preparation of arylpyridines as inhibitors of hedgehog signaling)

IT Carcinoma

(pancreatic adenocarcinoma; preparation of arylpyridines as inhibitors of hedgehog signaling)

IT Antitumor agents
Drug delivery systems
Human

```
(preparation of arylpyridines as inhibitors of hedgehog signaling)
IT
     Hedgehog protein
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (preparation of arylpyridines as inhibitors of hedgehog signaling)
ΙT
        (pulmonary small-cell, treatment; preparation of arylpyridines as inhibitors
        of hedgehog signaling)
     Sarcoma
IT
        (rhabdomyosarcoma, treatment; preparation of arylpyridines as inhibitors of
        hedgehog signaling)
IT
     Lung, neoplasm
        (small-cell carcinoma, treatment; preparation of arylpyridines as inhibitors
        of hedgehog signaling)
ΙT
     Biliary tract, neoplasm
     Esophagus, neoplasm
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     Stomach, neoplasm
        (treatment; preparation of arylpyridines as inhibitors of hedgehog
        signaling)
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(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
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(preparation of arylpyridines as inhibitors of hedgehog signaling) 879087-56-6P 879087-57-7P 879087-58-8P 879087-60-2P 879087-59-9P 879087-61-3P 879087-62-4P 879087-63-5P 879087-64-6P 879087-65-7P 879087-66-8P 879087-67-9P 879087-68-0P 879087-69-1P 879087-71-5P 879087-72-6P 879087-73-7P 879087-74-8P 879087-76-0P 879087-75-9P 879087-77-1P 879087-78-2P 879087-79-3P 879087-80-6P 879087-81-7P 879087-82-8P 879087-83-9P 879087-84-0P 879087-85-1P 879087-86-2P 879087-87-3P 879087-88-4P 879087-91-9P 879087-89-5P 879087-92-0P 879087-93-1P 879087-94-2P 879087-95-3P 879087-96-4P 879087-97-5P 879087-99-7P 879088-00-3P 879088-01-4P 879088-02-5P 879088-03-6P 879088-04-7P 879088-05-8P 879088-06-9P 879088-07-0P 879088-08-1P 879088-10-5P 879088-11-6P 879088-12-7P 879088-13-8P 879088-14-9P 879088-15-0P 879088-16-1P 879088-17-2P 879088-18-3P 879088-19-4P 879088-21-8P 879088-22-9P 879088-23-0P 879088-24-1P 879088-25-2P 879088-26-3P 879088-27-4P 879088-28-5P 879088-29-6P 879088-30-9P 879088-32-1P 879088-31-0P 879088-33-2P 879088-34-3P 879088-35-4P 879088-36-5P 879088-37-6P 879088-38-7P 879088-39-8P RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of arylpyridines as inhibitors of hedgehog signaling) IT 51-45-6, Histamine, reactions 60-24-2, 2-Mercaptoethanol 61-82-5, 3-Amino-1,2,4-triazole 62-23-7, 4-Nitrobenzoic acid 62-53-3, Aniline, reactions 67-51-6, 3,5-Dimethylpyrazole 75-03-6, Iodoethane Ethylamine, reactions 75-08-1, Ethanethiol 75-31-0, Isopropylamine, 75-33-2, 2-Propanethiol 75-64-9, tert-Butylamine, reactions reactions 78-77-3, 1-Bromo-2-methylpropane 78-81-9, Isobutylamine 79-14-1, Glycolic acid, reactions 79-19-6, Thiosemicarbazide 85-41-6, 95-72-7, 2-Chloro-1,4-dimethylbenzene Isoindoline-1,3-dione 2-Aminothiazole 98-88-4, Benzoyl chloride 100-09-4, 4-Methoxybenzoic 100-46-9, Benzylamine, reactions 103-67-3, N-Methyl-1-103-76-4, N-(2-Hydroxyethyl)piperazine phenylmethanamine 104-63-2104-78-9 106-93-4, 1,2-Dibromoethane 2-(Benzylamino)ethanol 107-03-9, 1-Propanethiol 107-10-8, Propylamine, reactions 108-49-6, 2,6-Dimethylpiperazine 108-91-8, Cyclohexanamine, reactions 109-01-3, N-Methylpiperazine 109-07-9, 2-Methylpiperazine 109-85-3, 2-Methoxyethanamine 110-85-0, Piperazine, reactions 110-89-4, Piperidine, reactions 110-91-8, Morpholine, reactions 118-91-2, 2-Chlorobenzoic acid 123-00-2, N-(3-Aminopropyl)morpholine 123-75-1, Pyrrolidine, reactions 123-90-0, Thiomorpholine 138-41-0, 141-43-5, Ethanolamine, reactions 4-Carboxybenzenesulfonamide 141-91-3, 2,6-Dimethylmorpholine 142-25-6, N,N,N'-Trimethylethylenediamine 156-87-6, Propanolamine 288-13-1, 1H-Pyrazole 288-36-8, 1H-1,2,3-Triazole 288-88-0, 1H-1,2,4-Triazole 4-(Trifluoromethylthio)benzoic acid 353-83-3, 2,2,2-Trifluoroethyl 393-55-5, 2-Fluoronicotinic acid 462-08-8, 3-Aminopyridine 497-25-6, 2-Oxazolidone 504-29-0, 2-Aminopyridine 504-78-9. Thiazolidine 505-66-8 506-59-2, Dimethylamine hydrochloride 513-38-2, 1-Iodo-2-methylpropane 584-13-4, 4-Amino-1,2,4-triazole 586-30-1, 3-Hydroxy-4-methylbenzoic acid 593-51-1, Methylamine 593-56-6 hydrochloride 594-44-5, Ethanesulfonyl chloride Bromoacetyl bromide 616-45-5, 2-Pyrrolidinone 618-36-0,

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1-Phenylethanamine
                     619-44-3, Methyl 4-iodobenzoate
                                                      619-65-8,
4-Cyanobenzoic acid 621-83-0, N-Benzylthiourea 660-68-4, Diethylamine
               683-57-8, 2-Bromoacetamide
hydrochloride
                                            704-45-0,
2-Methoxy-4-methylbenzoic acid 753-90-2, 2,2,2-Trifluoroethylamine
822-36-6, 4-Methylimidazole
                             922-67-8, Methyl propiolate
                                                            1068-47-9,
1-Mercapto-2-propanol
                        1122-71-0, (6-Methylpyridin-2-yl)methanol
1129-28-8, Methyl 3-(bromomethyl)benzoate
                                           1192-21-8,
5-Amino-1-methylpyrazole
                          1194-02-1, 4-Fluorobenzonitrile
                                                            1206-37-7.
4-[(Dimethylamino)sulfonyl]benzoic acid
                                          1606-49-1, 1,4,5,6-
Tetrahydropyrimidine
                       1664-40-0
                                   1679-64-7, 4-(Methoxycarbonyl)benzoic
       1779-81-3, 2-Amino-4,5-dihydrothiazole
                                                2038-03-1,
                        2417-72-3, Methyl 4-(bromomethyl)benzoate
2-Morpholinoethylamine
2510-36-3, 3,5-Dimethyl-4-isoxazolecarboxylic acid
                                                   2749-11-3,
(S)-2-Amino-1-propanol
                         2799-16-8
                                    2799-17-9, (S)-1-Amino-2-propanol
3144-09-0, Methanesulfonamide
                                3179-31-5, 4H-1,2,4-Triazole-3-thiol
3222-47-7, 6-Methylnicotinic acid
                                   3240-94-6, 4-(2-Chloroethyl)morpholine
3524-32-1, 1,3-Dimethyl-1H-pyrazol-5-amine
                                            3731-51-9,
                        3731-52-0, 3-Aminomethylpyridine 3731-53
4025-64-3, 3-(Chlorosulfonyl)benzoic acid
2-Aminomethylpyridine
                                                           3731-53-1,
4-Aminomethylpyridine
4066-41-5, 5-Acetylthiophene-2-carboxylic acid
                                                 4318-37-0,
1-Methyl-1, 4-diazepane
                        4318-76-7, 2,5-Diaminopyridine
                                                         4393-16-2,
(4-(Methylsulfonyl)phenyl)methaneamine
                                         4403-69-4
                                                    4795-29-3,
(Tetrahydrofuran-2-yl)methanamine
                                   4916-55-6, 3-(Bromomethyl)pyridine
hydrobromide
               5036-48-6, 1-(3-Aminopropyl)imidazole
                                                      5188-07-8, Sodium
                5308-25-8, 1-Ethylpiperazine
thiomethoxide
                                              5332-73-0,
                      5345-27-7, 3-(Methylsulfonyl)benzoic acid
3-Methoxypropylamine
5345-47-1, 2-Aminonicotinic acid
                                 5350-93-6, 6-Chloropyridin-3-amine
5382-16-1, 4-Piperidinol
                          5625-67-2, 3-Oxopiperazine
                                                        6068-72-0,
4-Cyanobenzoyl chloride
                          6232-88-8, 4-(Bromomethyl)benzoic acid
6283-25-6, 2-Chloro-5-nitroaniline 6302-65-4, Methyl 4-mercaptobenzoate
6482-24-2, 2-Bromoethyl methyl ether 6628-77-9, 2-Methoxy-5-
                7144-05-0, Piperidin-4-ylmethanamine
aminopyridine
                                                     7154-73-6,
N-(2-Aminoethyl)pyrrolidine 7170-01-6, 3-Methyl-1,2,4-triazole
7175-81-7
           7318-00-5, Ethyl 3-aminocrotonate 7663-77-6.
1-(3-Aminopropyl)-2-pyrrolidinone
                                   7697-27-0, 2-Bromo-4-methylbenzoic
       7720-39-0, 2-Aminoimidazole
acid
                                   10130-89-9, 4-Chlorosulfonylbenzoic
acid
       10147-37-2, 2-Propanesulfonyl chloride 10272-07-8,
3,5-Dimethoxyaniline
                     13324-11-3, Methyl 2-chloro-4-nitrobenzoate
13889-98-0, N-Acetylpiperazine 13952-84-6, sec-Butylamine 14678-05-8,
5-Aminoisoxazole
                  15448-47-2, reactions 15715-41-0, Diethyl
methylphosphonite
                   16088-62-3, (S)-Propylene oxide, reactions
16588-26-4, 3-Bromo-4-chloro-nitrobenzene 17213-57-9,
3,5-Dimethoxybenzoyl chloride 17570-98-8, 2-(Bromoacetyl)pyridine
hydrobromide 17616-04-5, 4-(1H-Imidazol-1-yl)benzoic acid 17874-79-2,
5-(Methoxycarbonyl)picolinic acid 18358-63-9, Methyl
4-(methylamino)benzoate 18643-86-2, Dimethyl 2-bromoterephthalate
19721-22-3, 3-Mercapto-1-propanol 20780-53-4 20780-54-5, (S)-Styrene
       20989-17-7, (S)-2-Amino-2-phenylethanol
                                                21035-59-6,
N-Methyl-1-(pyridin-2-yl)methanamine 21655-48-1, cis-2,6-
Dimethylpiperazine 23806-24-8, 3-Methyl-2-thiophenecarboxylic acid
24665-93-8, 2-Amino-4,5-dihydrooxazole
                                       24854-43-1, 4-Methyl-4H-1,2,4-
triazole-3-thiol
                 30609-80-4, 4-(2-Hydroxyethylthio)benzonitrile
31106-82-8, 2-(Bromomethyl)pyridine hydrobromide
                                                 31152-37-1, Thiazoline
33233-67-9
           38496-18-3, 2,6-Dichloronicotinic acid
                                                     40546-33-6,
3-(1H-Imidazol-4-yl)propan-1-amine
                                    41404-58-4, 5-Fluoro-2-bromopyridine
41838-46-4, 4-Amino-1-methylpiperidine
                                        42860-10-6, 3-Bromo-4-
chlorobenzoic acid 49773-20-8, 2-(Methylsulfonyl)ethanamine
50488-42-1, 5-Trifluoromethyl-2-bromopyridine 53250-83-2,
2-Chloro-4-methylsulfonylbenzoic acid
                                       54453-91-7, 4-Ethyl-2-
bromopyridine
              55276-43-2, 1-Methylsulfonylpiperazine
                                                        55715-03-2,
4-(Bromomethyl)-3-nitrobenzoic acid
                                     56613-80-0
                                                  57260-71-6
58757-38-3, 6-Chloronicotinoyl chloride
                                         60166-86-1, 5-
(Methylsulfonyl)thiophene-2-carboxylic acid 60702-69-4,
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2-Chloro-4-fluorobenzonitrile 67832-11-5, 4-Bromo-2-methylbenzonitrile
73781-91-6, Methyl 6-chloronicotinate 74879-18-8, (S)-2-Methylpiperazine
75336-86-6
            76003-29-7, tert-Butyl 3-oxopiperazine-1-carboxylate
78190-05-3, 4-(1H-Tetrazol-1-yl)benzoic acid
                                              78358-86-8,
                             82145-97-9, Methyl 4-((pyridin-2-
1-(2-Bromoethyl)-1H-pyrrole
ylthio)methyl)benzoate
                        87412-10-0, 5-Chloropyridin-2-yl
                            89938-62-5, 2-Chloro-5-(methylsulfonyl)benzoic
trifluoromethanesulfonate
       99636-32-5, (S)-1-Methoxy-2-propylamine
                                                 103249-79-2,
4-Methyl-2-phenyl-5-pyrimidinecarboxylic acid
                                                113023-73-7.
4-(1-Bromoethyl)benzoic acid
                              119071-57-7, 6-Chloropyridin-2-yl
trifluoromethanesulfonate
                            126456-43-7, (1S,2R)-1-Amino-2,3-dihydro-1H-
             133710-77-7, 2-(Pyrrolidin-2-yl)ethanamine
inden-2-ol
                                                          136030-00-7,
(1R,2S)-1-Amino-2,3-dihydro-1H-inden-2-ol
                                            147969-86-6,
4-((1-(tert-Butoxycarbonyl)piperidin-4-yl)methyl)benzoic acid
158580-87-1, Methyl 2-amino-4-(methylsulfonyl)benzoate
                                                         158581-07-8,
Methyl 4-(methylsulfonyl)-2-nitrobenzoate
                                            181772-16-7
                                                          192948-09-7,
1,2,3-Benzothiadiazole-5-carboxylic acid
                                           199535-00-7,
4-(Methylsulfonylmethyl)benzoic acid
                                       217073-76-2, 1-(4-Fluorophenyl)-5-
methyl-1H-pyrazole-4-carboxylic acid
                                       218777-23-2, 2-Pyridylzinc bromide
243853-14-7, 1-(4,5-Dihydro-1H-imidazol-2-yl)-3,5-dimethyl-1H-pyrazole
254910-60-6, 4-(3-Hydroxypropylthio)benzonitrile
                                                   257876-05-4,
5-Methyl-2-pyridylzinc bromide
                                 261635-98-7, 6-(Trifluoromethyl)-2-
methylpyridine-3-carbonyl chloride
                                     281232-20-0, 6-(1H-1,2,4-Triazol-1-
yl)pyridine-3-carboxylic acid
                               308795-91-7, 3-Methyl-2-pyridylzinc
          308795-93-9, 4-Methyl-2-pyridylzinc bromide
bromide
                                                        308795-98-4,
                                431888-57-2, 2-Chloro-4-
6-Methyl-2-pyridylzinc bromide
(methoxycarbonyl)benzoic acid
                                431888-59-4, 4-(tert-Butoxycarbonyl)-3-
                     573764-31-5, 4-Chloro-3-iodoaniline
chlorobenzoic acid
                                                          849774-31-8,
3-(Triisopropylsilyloxy)pyridine
                                   879088-63-8, 5-Acetyl-N-(4-chloro-3-
iodophenyl)thiophene-2-carboxamide
                                     879088-64-9
                                                   879088-65-0
879088-66-1
              879088-67-2
                            879088-68-3
                                          879088-69-4
                                                        879088-70-7.
5-Phenylpyridin-2-yl trifluoromethanesulfonate
                                                 879088-71-8
                                                               879088-72-9
879088-73-0, Methyl 4-((2-hydroxypropylthio)methyl)benzoate
                                                              879088-74-1
879088-75-2
              879088-76-3
                            879088-77-4, 4-((4H-1,2,4-Triazol-3-
ylsulfonyl)methyl)benzoic acid
                                 879088-78-5, 4-(((4-Methyl-4H-1,2,4-
triazol-3-yl)sulfinyl)methyl)benzoic acid
                                           879088-79-6.
4-(((4-Methyl-4H-1,2,4-triazol-3-yl)sulfonyl)methyl)benzoic acid
879088-80-9, 4-(Bromomethyl)-N-(3-(pyridin-2-yl)phenyl)benzamide
              879088-82-1, tert-Butyl 4-(bromomethyl)-2-chlorobenzoate
879088-81-0
879088-83-2, 4-Amino-N-(4-chloro-3-(pyridin-2-yl)phenyl)benzamide
879088-84-3, Methyl 2-chloro-4-mercaptobenzoate 879088-85-4,
4-(2-Bromoethylsulfonyl)benzonitrile
                                     879088-86-5
RL: RCT (Reactant); RACT (Reactant or reagent)
   (preparation of arylpyridines as inhibitors of hedgehog signaling)
              879088-88-7 879088-89-8, 4-((4H-1,2,4-Triazol-3-
ylsulfinyl)methyl)benzoic acid
RL: RCT (Reactant); RACT (Reactant or reagent)
   (preparation of arylpyridines as inhibitors of hedgehog signaling)
3556-86-3P, Methyl 3-hydroxy-4-methylbenzoate
                                               14186-60-8P, Dimethyl
2-methylterephthalate
                      46004-37-9P, Methyl 4-amino-2-chlorobenzoate
74534-15-9P, 1-Chloro-2-iodo-4-nitrobenzene 88089-94-5P, Methyl
4-(bromomethyl)-3-nitrobenzoate 116934-87-3P, 4-(Methoxycarbonyl)-3-
methylbenzoic acid 158580-55-3P
                                   199535-75-6P, Methyl
4-(methylsulfonylmethyl)-3-nitrobenzoate
                                          204568-74-1P, Methyl
                           220504-68-7P, Methyl 3-acetoxy-4-
3-acetoxy-4-methylbenzoate
(bromomethyl)benzoate
                       431888-58-3P
                                      879088-40-1P, 4-Chloro-3-(pyridin-2-
                 879088-41-2P
yl)nitrobenzene
                                879088-42-3P, 3-[3,5-
Bis(trifluoromethyl)phenyl]-1-bromopropane
                                            879088-43-4P.
4-(Ethylsulfonylmethyl)benzoic acid
                                    879088-44-5P, 4-(Dimethylcarbamoyl)-
2-methylbenzoic acid
                     879088-45-6P, 6-(tert-Butylcarbamoyl)nicotinic acid
879088-46-7P, 6-(Pyridin-2-ylmethylcarbamoyl)nicotinic acid
879088-47-8P, 6-(Benzylcarbamoyl)nicotinic acid
                                                 879088-48-9P.
6-(6-Methoxypyridin-3-ylcarbamoyl)nicotinic acid 879088-49-0P, Methyl
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4-((2-hydroxypropylsulfonyl)methyl)benzoate 879088-50-3P,
     4-((2-Hydroxypropylsulfonyl)methyl)benzoic acid 879088-51-4P
     879088-52-5P
                  879088-53-6P 879088-54-7P
                                                  879088-55-8P, Methyl
     3-acetoxy-4-(methylsulfonylmethyl)benzoate
                                                  879088-56-9P,
     3-Hydroxy-4-(methylsulfonylmethyl)benzoic acid
                                                      879088-57-0P
     879088-58-1P 879088-59-2P, 4-(Methylsulfonylmethyl)-3-nitrobenzoic acid
     879088-60-5P
                    879088-61-6P
                                  879088-62-7P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (preparation of arylpyridines as inhibitors of hedgehog signaling)
     ANSWER 2 OF 12 CAPLUS COPYRIGHT 2007 ACS on STN
     Compounds for inhibiting copper-containing amine oxidases and their use in
     inflammatory disease
     2006:116947 CAPLUS
     144:205758
     Compounds for inhibiting copper-containing amine oxidases and their use in
     inflammatory disease
     Olarte, Antonio Zorzano; Mian, Alec; Clauzel, Luc Marti; Exposito, Miriam
     Royo; Font, Francesc Yraola; Palomera, Fernando Albericio
     Genmedica Therapeutics SL, Spain
     PCT Int. Appl., 78 pp.
     CODEN: PIXXD2
     Patent
    English
FAN.CNT 1
    PATENT NO.
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    WO 2006013209
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                                                                  20050802
    WO 2006013209
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                               20060615
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            GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ,
            LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA,
            NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK,
            SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU,
            ZA, ZM, ZW
        RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
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            CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
            GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
            KG, KZ, MD, RU, TJ, TM
                                           US 2004-598010P
                                                               P 20040802
    MARPAT 144:205758
    The present invention is directed to inhibitors of copper-containing amine
    oxidases (E.C.1.4.3.6) including semicarbazide-sensitive amine oxidase
    (SSAO; also known as vascular adhesion protein- 1, VAP-I), and their
    therapeutic use in inflammatory diseases, diabetes and its associated
    complications, atherosclerosis, neurodegenerative diseases, obesity,
    hypertension and cancer.
    Inflammation
       (Crohn's disease; compds. for inhibiting copper-containing amine oxidases
       and their uses)
    Intestine, disease
       (Crohn's; compds. for inhibiting copper-containing amine oxidases and their
       uses)
    Blood vessel, disease
       (Raynaud's phenomenon; compds. for inhibiting copper-containing amine
       oxidases and their uses)
    Tinea (skin disease)
       (Tinea versicolor, pityriasis rosea; compds. for inhibiting
       copper-containing amine oxidases and their uses)
    Proteins
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RL: BSU (Biological study, unclassified); BIOL (Biological study) (VAP-1 (vascular adhesion protein 1), inhibitors; compds. for inhibiting copper-containing amine oxidases and their uses) Respiratory distress syndrome (acute; compds. for inhibiting copper-containing amine oxidases and their uses) Adipose tissue (adipocyte, dysfunction; compds. for inhibiting copper-containing amine oxidases and their uses) Inflammation Spinal column, disease (ankylosing spondylitis; compds. for inhibiting copper-containing amine oxidases and their uses) Antiarteriosclerotics (antiatherosclerotics; compds. for inhibiting copper-containing amine oxidases and their uses) Mouth, disease (aphthous ulcer; compds. for inhibiting copper-containing amine oxidases and their uses) Ulcer (aphthous; compds. for inhibiting copper-containing amine oxidases and their uses) Inflammation Stomach, disease (atrophic gastritis; compds. for inhibiting copper-containing amine oxidases and their uses) (bacterial, Helicobacter pylori; compds. for inhibiting copper-containing amine oxidases and their uses) Bronchi, disease Inflammation (bronchitis; compds. for inhibiting copper-containing amine oxidases and their uses) Ischemia (cardiac; compds. for inhibiting copper-containing amine oxidases and their uses) (central origin; compds. for inhibiting copper-containing amine oxidases and their uses) Lung, disease (chronic obstructive pulmonary disease; compds. for inhibiting copper-containing amine oxidases and their uses) Inflammation Lung, disease (chronic pneumonitis; compds. for inhibiting copper-containing amine oxidases and their uses) Dermatitis (chronic; compds. for inhibiting copper-containing amine oxidases and their uses) Alzheimer's disease Analgesics Anti-Alzheimer's agents Anti-inflammatory agents Antiarthritics Antiasthmatics Antidiabetic agents Antiglaucoma agents Antihypertensives Antiobesity agents

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Antiparkinsonian agents

Antirheumatic agents

Antipyretics

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Antitumor agents
Antiulcer agents
Arthritis
Asthma
Atherosclerosis
Bacteremia
Blood vessel, disease
Bone resorption
Bone resorption inhibitors
Celiac disease
Cystic fibrosis
Diabetes mellitus
Digestive tract, disease
Disease, animal
Drug delivery systems
Eczema
Endotoxemia
Fever and Hyperthermia
Gastrointestinal agents
Glaucoma (disease)
Gout
Human
Hypertension
Immune disease
Inflammation
Meningitis
Multiple sclerosis
Neoplasm
Nervous system agents
Obesity
Osteoarthritis
Parkinson's disease
Periodontium, disease
Psoriasis
Rheumatoid arthritis
Sepsis
   (compds. for inhibiting copper-containing amine oxidases and their uses)
Carbohydrate metabolism
RL: BSU (Biological study, unclassified); BIOL (Biological study)
   (compds. for inhibiting copper-containing amine oxidases and their uses)
Eye, disease
Inflammation
   (conjunctivitis; compds. for inhibiting copper-containing amine oxidases
   and their uses)
Nervous system, disease
   (degeneration; compds. for inhibiting copper-containing amine oxidases and
   their uses)
Hydroxamic acids
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
   (derivs.; compds. for inhibiting copper-containing amine oxidases and their
   uses)
Lung, disease
   (farmer's lung; compds. for inhibiting copper-containing amine oxidases and
   their uses)
Inflammation
Stomach, disease
   (gastritis, varioliform; compds. for inhibiting copper-containing amine
   oxidases and their uses)
Gingiva, disease
Inflammation
   (gingivitis; compds. for inhibiting copper-containing amine oxidases and
   their uses)
```

ΙT

IT

IT

IT

IT

IT

IT

IT Inflammation Intestine, disease (ileitis; compds. for inhibiting copper-containing amine oxidases and their Helicobacter pylori IT (infection; compds. for inhibiting copper-containing amine oxidases and their uses) ΙT Central nervous system, disease (inflammation; compds. for inhibiting copper-containing amine oxidases and their uses) ITPain (inflammatory pain; compds. for inhibiting copper-containing amine oxidases and their uses) ΙT Intestine, disease (inflammatory; compds. for inhibiting copper-containing amine oxidases and their uses) IT Reperfusion (injury, ischemia; compds. for inhibiting copper-containing amine oxidases and their uses) ΙT Intestine, disease (irritable bowel syndrome; compds. for inhibiting copper-containing amine oxidases and their uses) IT Heart, disease (ischemia; compds. for inhibiting copper-containing amine oxidases and their uses) IT Skin, disease (lichen planus; compds. for inhibiting copper-containing amine oxidases and their uses) IT Angiogenesis (neovascularization, retinal; compds. for inhibiting copper-containing amine oxidases and their uses) IT Nerve, disease Pain (neuralgia; compds. for inhibiting copper-containing amine oxidases and their uses) ΙT Nerve, disease (neuropathy; compds. for inhibiting copper-containing amine oxidases and their uses) IT Eye, disease Inflammation (ophthalmitis; compds. for inhibiting copper-containing amine oxidases and their uses) ITInflammation Pancreas, disease (pancreatitis; compds. for inhibiting copper-containing amine oxidases and their uses) ΤT Ulcer (peptic; compds. for inhibiting copper-containing amine oxidases and their uses) IT Inflammation Lung, disease (pneumonitis; compds. for inhibiting copper-containing amine oxidases and their uses) IT Arthritis (psoriatic arthritis; compds. for inhibiting copper-containing amine oxidases and their uses) IT Esophagus, disease Inflammation (reflux esophagitis; compds. for inhibiting copper-containing amine oxidases and their uses) IT

(reperfusion, ischemia; compds. for inhibiting copper-containing amine

oxidases and their uses)

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IT
     Eye, disease
        (retina, neovascularization; compds. for inhibiting copper-containing amine
        oxidases and their uses)
IT
     Shock (circulatory collapse)
        (septic; compds. for inhibiting copper-containing amine oxidases and their
        uses)
     Inflammation
IT
     Spinal column, disease
        (spondylitis, rheumatoid; compds. for inhibiting copper-containing amine
        oxidases and their uses)
IT
     Brain, disease
        (stroke; compds. for inhibiting copper-containing amine oxidases and their
IT
     Digestive tract, disease
        (ulcer, peptic; compds. for inhibiting copper-containing amine oxidases and
        their uses)
IT.
     Foot
        (ulcer; compds. for inhibiting copper-containing amine oxidases and their
        uses)
IT
     Inflammation
     Intestine, disease
        (ulcerative colitis; compds. for inhibiting copper-containing amine
        oxidases and their uses)
IT
     Eye, disease
     Inflammation
        (uveitis; compds. for inhibiting copper-containing amine oxidases and their
        uses)
IT
     875518-37-9P
     RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
     (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
     (Uses)
        (compds. for inhibiting copper-containing aminle oxidases and their uses)
IT
     116408-48-1P
                    130289-49-5P
                                    154737-59-4P
                                                   327037-09-2P
                                                                  327037-34-3P
     875518-38-0P
                    875518-39-1P
                                    875518-40-4P
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                                                                  875518-42-6P
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                                    875518-45-9P
                                                   875518-46-0P
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     RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
     (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
     (Uses)
        (compds. for inhibiting copper-containing amine oxidases and their uses)
IT
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                                                875518-87-9
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     RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (compds. for inhibiting copper-containing amine oxidases and their uses)
ΙT
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                                  875521-17-8
                                                875521-18-9
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     875521-20-3
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                                                               875521-39-4
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     875521-60-1
                   875521-61-2
                                  875521-62-3
     RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (compds. for inhibiting copper-containing amine oxidases and their uses)
IT
     108-30-5, Succinic anhydride, reactions
                                                5470-11-1
                                                            26588-35-2,
     Biphenylsulfonyl chloride
                                 160450-13-5
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (compds. for inhibiting copper-containing amine oxidases and their uses)
IT
     9001-53-0, Copper-containing amine oxidase
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (inhibitors, Semicarbazide-sensitive; compds. for inhibiting
        copper-containing amine oxidases and their uses)
L8
     ANSWER 3 OF 12 CAPLUS COPYRIGHT 2007 ACS on STN
     Preparation of tetrahydronaphthalene hydroxamates and benzamides as
TΙ
     histone deacetylase (HDAC) inhibitors.
AN
     2005:516308 CAPLUS
DN
     143:43695
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Preparation of tetrahydronaphthalene hydroxamates and benzamides as histone deacetylase (HDAC) inhibitors.

IN Leblond, Bertrand; Beausoleil, Eric
PA Exonhit Therapeutics S.A., Fr.
SO Eur. Pat. Appl., 50 pp.
CODEN: EPXXDW
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DT Patent LA English

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| | PATENT NO. | | | | | KIND DATE | | | | APPL | ICAT | | DATE | | | | | | | |
|----|------------|-----------|-----|-----|-----|-----------|-------------|------|----------------|------|----------|----------|-----------------|-----|----------|------------|-------|-----|--|--|
| PI | EP | 1541 | 549 | | | A1 | Al 20050615 | | 0615 | |
EP 2 |
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2931 | 43 | 20031212 | | | | | |
| | | R: | ΑT, | | | | | ES, | | | | | | | | | | | | |
| | | | ΙE, | SI, | LT, | LV, | FI, | RO, | MK, | CY, | AL, | TR, | BG, | CZ, | EE, | HU, | SK | · | | |
| | WO | 2005 | | | | | | | | | | | | | | 20041210 | | | | |
| | | W: | ΑE, | AG, | | | | ΑU, | | | | | | | | | | | | |
| | | | | | | | | DE, | | | | | | | | | | | | |
| | | | GE, | GH, | GM, | HR, | HU, | ID, | IL, | IN, | IS, | JP, | KE, | KG, | KP, | KR, | KZ, | LC, | | |
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| | | | ТJ, | TM, | TN, | TR, | TT, | TZ, | UA, | ŪG, | US, | UZ, | VC, | VN, | YU, | ZA, | ZM, | ZW | | |
| | | RW: | BW, | GH, | GM, | ΚE, | LS, | MW, | MZ, | NA, | SD, | SL, | SZ, | TZ, | ŪG, | ZM, | ZW, | AM, | | |
| | | | ΑZ, | BY, | KG, | ΚZ, | MD, | .RU, | ТJ, | TM, | AT, | BE, | BG, | CH, | CY, | CZ, | DE, | DK, | | |
| | | | EE, | ES, | FI, | FR, | GB, | GR, | HU, | ΙE, | IS, | IT, | LT, | LU, | MC, | NL, | PL, | PT, | | |
| | | | RO, | SE, | SI, | SK, | TR, | BF, | ВJ, | CF, | CG, | CI, | CM, | GA, | GN, | GQ, | GW, | ML, | | |
| | | | MR, | ΝE, | SN, | TD, | ΤG | | | | | | | | | | | | | |
| | | | | | | | | | | | | | | | | A 20031212 | | | | |
| | EΡ | P 1692097 | | | | | | | EP 2004-806498 | | | | | | | | | | | |
| | | R: | | | | | | ES, | | | | | | | | | MC, | PT, | | |
| | | | ΙE, | SI, | LT, | FI, | RO, | CY, | TR, | | | | | | | | | | | |
| | | | | | | | | | | | | | | | | A 20 | 00312 | 212 | | |
| | | | | | _ | | | | | 1 | WO 20 | 004-3 | IB43 | 34 | 1 | W 20 | 00412 | 210 | | |

OS MARPAT 143:43695 GI

Title compds. [I; R = CONR7R8, COCONR8R9, COCONHMe, COCF3, etc.; R7 = OH, OR9, 2-aminophenyl; R8, R9 = H, alkyl; X1 = C, O, N, S; R1, R2 = null, H, alkyl, 1-2 O; X2, X3 = CH, O, N; X2X3 = S, O, N; X4 = N, CH; R3-R5 = H, OH, NH2, halo, alkyl, perfluoroalkyl, etc.; L = alkylene, alkenylene, alkynylene, (aromatic) cycloalkyl, O, CO, CONH, CF2CONH, SO2NH, NMeSO2, etc.], were prepared Thus, 4-[2,2-difluoro-2-(5,5,8,8-tetramethyl-5,6,7,8-tetrahydronaphthalen-2-yl)acetylamino]benzoic acid (preparation given) was stirred with SOC12 and cat. DMF at 0° for 1 h. The residue in CH2C12 was added to a mixture prepared from hydroxylamine hydrochloride, H2O, and Et3N in THF at 0° followed by stirring at 0° for 10 min. and at room temperature for 17.75 h to give 33.4% 4-[2,2-difluoro-2-(1,2,3,4-tetrahydro-1,1,4,4-tetramethylnaphthalen-7-yl)acetamido]-N-hydroxybenzamide (EHT 9299). The latter showed HDAC inhibitory activity with IC50 = 424 nM.

IT Nervous system, disease (Huntington's chorea, treatment; preparation of tetrahydronaphthalene

hydroxamates and benzamides as histone deacetylase inhibitors) ΙT Nervous system, disease (amyotrophic lateral sclerosis, treatment; preparation of tetrahydronaphthalene hydroxamates and benzamides as histone deacetylase inhibitors) ΙT Intestine, neoplasm (colon, treatment; preparation of tetrahydronaphthalene hydroxamates and benzamides as histone deacetylase inhibitors) IT Liver, disease (fibrosis, treatment; preparation of tetrahydronaphthalene hydroxamates and benzamides as histone deacetylase inhibitors) IT Neoplasm Neoplasm (head and neck, treatment; preparation of tetrahydronaphthalene hydroxamates and benzamides as histone deacetylase inhibitors) IT (hepatic, treatment; preparation of tetrahydronaphthalene hydroxamates and benzamides as histone deacetylase inhibitors) IT Nerve, disease (ischemia, treatment; preparation of tetrahydronaphthalene hydroxamates and benzamides as histone deacetylase inhibitors) ΙT (neuronal, treatment; preparation of tetrahydronaphthalene hydroxamates and benzamides as histone deacetylase inhibitors) IT Lymphoma (non-Hodgkin's, treatment; preparation of tetrahydronaphthalene hydroxamates and benzamides as histone deacetylase inhibitors) IT Drug delivery systems Human (preparation of tetrahydronaphthalene hydroxamates and benzamides as histone deacetylase inhibitors) IT Acute promyelocytic leukemia Alzheimer's disease Bladder, neoplasm Cirrhosis Head and Neck, neoplasm Head and Neck, neoplasm Liver, neoplasm Lung, neoplasm Mammary gland, neoplasm Melanoma Multiple sclerosis Neoplasm Ovary, neoplasm Pancreas, neoplasm Parkinson's disease Prostate gland, neoplasm Psoriasis (treatment; preparation of tetrahydronaphthalene hydroxamates and benzamides as histone deacetylase inhibitors) IT 149647-78-9P RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation) (EHT 0648, reference compound; preparation of tetrahydronaphthalene hydroxamates and benzamides as histone deacetylase inhibitors) IT 149648-52-2P RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (Suberanilic acid; preparation of tetrahydronaphthalene hydroxamates and benzamides as histone deacetylase inhibitors) ΙT 853728-52-6P, N-(4-(Hydroxycarbamoyl)phenyl)-5,6,7,8-tetrahydro-5,5,8,8-

tetramethylnaphthalene-2-carboxamide 853728-53-7P, N-(4-(2-

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Aminophenylcarbamoyl)phenyl)-5,6,7,8-tetrahydro-5,5,8,8-tetramethyl-
     naphthalene-2-carboxamide 853728-54-8P
                                               853728-55-9P
     853728-56-0P
                     853728-57-1P, 4-(2,2-Difluoro-2-(1,2,3,4-tetrahydro-1,1,4,4-
     tetramethylnaphthalen-7-yl)acetamido)-N-hydroxybenzamide 853728-58-2P.
     3-(2,2-Difluoro-2-(1,2,3,4-tetrahydro-1,1,4,4-tetramethylnaphthalen-7-
     yl)acetamido)-N-hydroxybenzamide
                                         853728-59-3P, 4-((2,2-Difluoro-2-
     (1,2,3,4-\text{tetrahydro}-1,1,4,4-\text{tetramethylnaphthalen}-7-yl) acetamido) methyl) -N-
                       853728-60-6P 853728-61-7P, N-(4-
     hydroxybenzamide
     Hydroxycarbamoylphenyl)-N'-(5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-
     naphthalen-2-yl)oxalamide
     RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
     (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
     (Uses)
        (claimed compound; preparation of tetrahydronaphthalene hydroxamates and
        benzamides as histone deacetylase inhibitors)
IT
     56-91-7, 4-Aminomethylbenzoic acid
                                           62-53-3, Aniline, reactions
     95-54-5, 1,2-Phenylenediamine, reactions
                                                  505-48-6, Suberic acid
     540-37-4, 4-Iodophenylamine 619-45-4, Methyl 4-aminobenzoate Ethyl bromodifluoroacetate 1571-08-0, Methyl 4-formylbenzoate
                                                                        667-27-6,
     1679-64-7, Terephthalic acid monomethyl ester
                                                       4518-10-9, Methyl
     3-aminobenzoate
                       5781-53-3, Methyl oxalyl chloride
                                                             6683-46-1,
     1,1,4,4-Tetramethyl-1,2,3,4-tetrahydronaphthalene
                                                           6683-48-3,
     1,1,4,4,6-Pentamethyl-1,2,3,4-tetrahydronaphthalene
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (preparation of tetrahydronaphthalene hydroxamates and benzamides as histone
        deacetylase inhibitors)
IT
     10521-06-9P, 2,9-Oxonanedione
                                      18469-52-8P, Methyl 4-
     (aminomethyl)benzoate
                              92050-16-3P, 5,5,8,8-Tetramethyl-5,6,7,8-
     tetrahydro-naphthalen-2-ylamine
                                        94497-53-7P
                                                       102121-54-0P
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                    102121-60-8P
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     tetrahydro-naphthalene-2-carboxylic acid 119435-90-4P
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     119436-53-2P
                    119454-82-9P
                                    121866-06-6P
                                                   168301-01-7P
                                                                   168301-02-8P
     853728-62-8P
                    853728-63-9P
                                    853728-64-0P
                                                    853728-65-1P
                                                                   853728-66-2P
     853728-67-3P
                    853728-68-4P
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                                                                   853728-71-9P
     853728-72-0P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (preparation of tetrahydronaphthalene hydroxamates and benzamides as histone
        deacetylase inhibitors)
RE.CNT
              THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
              ALL CITATIONS AVAILABLE IN THE RE FORMAT
rs
     ANSWER 4 OF 12 CAPLUS COPYRIGHT 2007 ACS on STN
     Preparation of arylhydroxamates as elastase and collagenase expression
TI
     inhibitors for preventing skin aging.
AN
     2005:182616 CAPLUS
     142:279954
DN
ΤI
     Preparation of arylhydroxamates as elastase and collagenase expression
     inhibitors for preventing skin aging.
IN
     Rho, Ho Sik; Baek, Heung Soo; Kim, Su Jong; Kim, Su Nam; Chae, Byung Geun;
     Lee, Byoung Seok; Kim, Bae Hwan; Choi, Gyu Ho; Son, Eui Dong; Lee, Hae
     Kwang; Lee, Hye Won; Cho, Jun-cheol; Kim, Duck Hee; Chang, Ih Seop; Lee,
     Ok Sub
PA
     Amorepacific Corporation, S. Korea
SO
     PCT Int. Appl., 58 pp.
     CODEN: PIXXD2
DT
     Patent
     English
LΑ
FAN.CNT 1
     PATENT NO.
                         KIND
                                DATE
                                             APPLICATION NO.
                                                                     DATE
PΙ
     WO 2005019162
                          A1
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                                             WO 2004-KR2143
                                                                     20040826
         W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
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CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
        GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KZ, LC, LK,
        LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO,
        NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ,
        TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
    RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
        AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
        EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
        SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
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KR 2006005892
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                                       EP 2004-774404
                                                               20040826
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                                       KR 2004-20401
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                                                               20040325
                                       KR 2004-54886
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                                                               20040714
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CN 1839115
                     Α
                           20060927
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US 2006252834
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                                       WO 2004-KR2143
                                                            W 20040826
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OS MARPAT 142:279954 GI

$$R^3$$
 N
 OH
 $Q^1 = R^5$
 R^4
 $Q^1 = R^5$
 R^4
 R^4
 R^2
 R^3
 R^4
 R

AB Title compds. [I; R1 = adamantyl, Q1; R5, R6 = H, alkyl, cycloalkyl; R2 = CONH, NHCO, CONR7, NR7CO; R7 = alkyl; R3 = (CH)n; n = 0, 1; R4 = H, alkyl], were prepared Thus, 4-(phenylcarbonylamino)benzoic acid (preparation given) in pyridine at 10° was treated dropwise with Et chloroformate followed by stirring for 2 h at room temperature to give the anhydride. This was added to NH2OH.HCl in pyridine at 10° followed by stirring for 30 min. to give 65% N-[4-(N-hydroxycarbamoyl)phenyl]benzam ide. The latter reduced collagenase expression in vitro to 78% of controls, vs. 85% for retinol.

(creams, wrinkle-preventing; preparation of arylhydroxamates as elastase and collagenase expression inhibitors for preventing skin aging)
Retinoid receptors

RL: BSU (Biological study, unclassified); BIOL (Biological study) (ligands; preparation of arythydroxamates as elastase and collagenase expression inhibitors for preventing skin aging)

Cosmetics
(preparation of arylhydroxamates as elastase and collagenase expression inhibitors for preventing skin aging)

IT Hydroxamic acids

ΙT

IT

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RL: COS (Cosmetic use); SPN (Synthetic preparation); BIOL (Biological
     study); PREP (Preparation); USES (Uses)
        (preparation of arylhydroxamates as elastase and collagenase expression
        inhibitors for preventing skin aging)
                             9004-06-2, Elastase
IT
     9001-12-1, Collagenase
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (expression inhibitors; preparation of arylhydroxamates as elastase and
        collagenase expression inhibitors for preventing skin aging)
ΙT
     149648-29-3P
                   475557-69-8P
                                  475557-71-2P
                                                  847249-45-0P
                    847249-49-4P
     847249-48-3P
                                   847249-51-8P
                                                  847249-53-0P
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     847249-57-4P
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     RL: COS (Cosmetic use); SPN (Synthetic preparation); BIOL (Biological
     study); PREP (Preparation); USES (Uses)
        (preparation of arylhydroxamates as elastase and collagenase expression
        inhibitors for preventing skin aging)
     62-53-3, Aniline, reactions 65-85-0, Benzoic acid, reactions
IT
                           98-73-7, 4-tert-Butylbenzoic acid
     3,4-Dimethylaniline
     3-Methylbenzoic acid
                            99-88-7, 4-Isopropylaniline
                                                          99-94-5,
                            104-13-2, 4-Butylaniline
     4-Methylbenzoic acid
                                                      106-49-0,
     4-Methylaniline, reactions
                                 108-44-1, 3-Methylaniline, reactions
     536-66-3, 4-Isopropylbenzoic acid 589-16-2, 4-Ethylaniline
     3,4-Dimethylbenzoic acid 619-45-4, Methyl 4-aminobenzoate 619-64-7,
     4-Ethylbenzoic acid
                          768-94-5, Adamantanamine
                                                      769-92-6,
     4-tert-Butylaniline
                           1679-64-7, Monomethylterephthalate
                                                                2438-05-3.
     4-Propylbenzoic acid
                          2696-84-6, 4-Propylaniline
                                                         3814-10-6
                                                                   4229-44-1,
     N-Methylhydroxylamine hydrochloride 5470-11-1
                                                       20651-71-2,
                           39552-81-3, 4-Aminophenylacetic acid methyl ester
     4-Butylbenzoic acid
     42862-36-2, Adamantanecarboxylic acid 102121-29-9
                                                           102121-30-2
     121768-34-1
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     847250-80-0
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (preparation of arylhydroxamates as elastase and collagenase expression
        inhibitors for preventing skin aging)
IT
     93-97-0P, Benzoic anhydride
                                 582-80-9P
                                               39799-73-0P
     847250-53-7P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (preparation of arylhydroxamates as elastase and collagenase expression
        inhibitors for preventing skin aging)
RE.CNT 2
              THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
              ALL CITATIONS AVAILABLE IN THE RE FORMAT
L8
     ANSWER 5 OF 12 CAPLUS COPYRIGHT 2007 ACS on STN
TI
     Preparation of thiophenedicarboxamides and related compounds as histone
     deacetylase (HDAC) inhibitors.
AN
     2003:43028 CAPLUS
DN
     138:106596
TI
     Preparation of thiophenedicarboxamides and related compounds as histone
     deacetylase (HDAC) inhibitors.
IN
     Leser-Reiff, Ulrike; Sattelkau, Tim; Zimmermann, Gerd
     Hoffman-La Roche, Inc., Germany
PA
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U.S. Pat. Appl. Publ., 19 pp. so CODEN: USXXCO

DTPatent LΑ English FAN.CNT 1

| FAN. | FAN.CNT 1 | | | | | | | | | | | | | | | | | | | |
|------|-----------|--------------|-------|------|------|------------|-----------|-------|--------------|-----|----|----------|-------|----------------------|-------|------------|--------|------|----------------------|------|
| | PA' | rent | NO. | | | KIN | | DATE | : | | AP | PL: | ICAT | ION | NO. | | | DA | TE | |
| PI | | 2003
6784 | | 57 | | A1
B2 | | | 0116
0831 | | US | 20 | 002- | 1676 | 77 | | | 20 | 020 | 511 |
| | CA | 2449 | 804 | | | A1 | | 2003 | 0213 | | CA | 20 | 002- | 1144
2449 | 804 | | A | 20 | 010
020 | 513 |
| | | 2003 | | | | A2 | | 2003 | 0213 | | WO | 20 | 002- | 1144
EP64
EP64 | 88 | | A
W | 20 | 0106
0206
0206 | 513 |
| | WO | 2003 | | | | A 3 | | 2003 | 0918 | | | | | | | | | | | |
| | | W: | AE, | AG, | AL, | AM, | AT, | AU, | AZ, | BA, | Bl | В, | BG, | BR, | BY, | BZ, | CP | ١, | CH, | CN, |
| | | | GM | UK, | υ, | CA, | DE, | DK, | DM, | DZ, | E(| C, | EE, | ES, | FI, | GB, | GI | , | GE, | GH, |
| | | | LS | T.TP | T.II | I.V | MΣ
TT, | MD | IS,
MG, | ME, | M | L, | KG, | KP, | KK, | KZ, | TC | , | LK, | LR, |
| | | | PL. | PT. | RO. | RU. | SD. | SE. | SG, | ST | 21 | N, | ST. | MA,
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| | | | UA, | UG, | UZ, | VN. | YU. | ZA. | ZM, | ZW, | 51 | , | υц, | 10, | 111, | 111, | 11 | ', | 11, | 14, |
| | | RW: | GH, | GM, | KE, | LS, | MW, | MZ, | SD, | SL, | SZ | Z. | TZ. | UG. | ZM. | ZW. | ΑM | [. j | A7. | BY. |
| | | | KG, | ΚZ, | MD, | RU, | ТJ, | TM, | AT, | ΒE, | CI | Η, | CY, | DE, | DK, | ES, | FΙ | , | FR, | GB, |
| | | | GR, | ΙE, | IT, | LU, | MC, | NL, | PT, | SE, | T | R, | BF, | ВJ, | CF, | CG, | CI | , (| CM, | GΑ, |
| | | | GN, | GQ, | GW, | ML, | MR, | ΝE, | SN, | | | | | | | | | | | |
| | מש | 1401 | 024 | | | 3.0 | | 0004 | 0001 | | | | | 1144 | | i | | | 0106 | |
| | | 14018 | | | | A2
B1 | | | 0331 | | EΡ | 20 | J02- | 7914 | 36 | | | 20 | 0206 | 513 |
| | DE | R: | | BE | CH | | | | 1025
FR, | CP | CT | , | τm | T T | T T T | 117 | c E | | | D.M. |
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Γ. | TI, | пт, | ъυ, | иL, | 35 | , 1 | MC, | PI, |
| | | • | | , | _ , | | , | , | | | | | 11449 | 96 - | ; | Δ | 200 | 0106 | 15 | |
| | | | | | | | | | | | | | EP648 | | | | | 0206 | | |
| | CN | N 1516697 | | | Α | | 2004 | 0728 | | | | | 3120 | | | | | 0206 | | |
| | | | , | | | | | | | | | | | 11449 | | 7 | | | 0106 | |
| | BR | 20020 | 01042 | 24 | | Α | | 2004 | 0817 | | BR | 20 | 002-3 | 10424 | 1 | | | 200 | 206 | 13 |
| | | | | | | | | | | | | | | L1449 | | | | | 0106 | |
| | Ν'n | 52987 | 7.4 | | | 70 | | 2004 | 1004 | | | | | EP648 | | V | | | 0206 | |
| | 14.2 | J290 . | / 4 | | | A | • | 2004 | 1224 | | | | | 52987
L1449 | | , | | | 0206 | |
| | JР | 20055 | 50264 | 41 | | т | | 2005 | 0127 | | | | | 51704 | | F | | | 0106
0206 | |
| | | | | | | - | | | 012, | | | | | 11449 | | . 1 | | | 106 | |
| | | | | | | | | | | | | | | EP648 | | | | | 206 | |
| | ΑT | 34356 | 59 | | | T | 2 | 2006 | 1115 | | | | | 79143 | | | | | 206 | |
| | | | | | | | | | | | | | | L1449 | | 7 | A | 200 | 106 | 15 |
| | RU | 22895 | 080 | | | C2 | - 7 | 2006 | 1220 | | | | | L3757 | | | | | 206 | |
| | | | | | | | | | | | | | | 11449 | | | | | 106 | |
| | 7. A | 20030 | ากจวล | 50 | | Α | | 2005 | าววล | | | |)02-E | EP648 | 88 | V | | | 206 | |
| | ٠. ٢ | 20050 | 002 | ,, | | Λ. | • | 2005 | 0220 | | | | | 1449 | 16 | 7 | | |)311
)106 | |
| | IN | 20030 | CN019 | 981 | | Α | 2 | 2006 | 0106 | | | | | N198 | | • | | |)312 | |
| | | | | | | | | | | | | | | 1449 | | I | | | 106 | |
| | | | | | | | | | | | | | | EP648 | | | | | 206 | |
| | BG | 10845 | 50 | | | Α | 2 | 20050 | 0131 | | | | | .0845 | | | | | 312 | |
| | | 00045 | | | | | | | | | | | | .1449 | | P | | | 106 | |
| | US | 20042 | 21486 | 2 | | A1 | 2 | 2004 | 1028 | | | | | 34716 | | | | | 405 | |
| | | | | | | | | | | | | | | 1449 | | | | | 106 | |
| | HK | 10657 | 787 | | | A1 | , | 20063 | 1117 | | | | | 6767 | | F | | | 206 | |
| | 1111 | 1000 | , , , | | | ΛŢ | 4 | .000. | L T T / | | | | | .0849
.1449 | | 7 | | | 1106 | |
| | | | | | | | | | | | | | | 1445
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)206 | |
| os | MAR | PAT 1 | 138:1 | 0659 | 96 | | | | | | - | | | -1 5 10 | . • | • | • | | .200 | 13 |

OS MARPAT 138:106596
AB HONHCOACONR1R2 [A = (substituted) Ph, thienyl; R1, R2 = H, (substituted) alkyl, carbocyclyl, heterocyclyl; NR1R2 = (substituted) 3-6 membered

ring], were prepared Thus, thiophene-2,5-dicarboxylic acid monomethyl ester and N-methylmorpholine in CH2Cl2 at -10° were treated with 1-aminomethylnaphthalene in CH2Cl2; the mixture was stirred 90 min to give 58% monoamide. This was stirred with NH2OH.HCl and NaOMe in MeOH for 4 h to give thiophene-2,5-dicarboxylic acid 2-hydroxyamide 5-[(naphthalen-1-ylmethyl)amide]. Tested title compds. inhibited HT-29 tumor cell growth with IC50 = $0.02-0.17 \mu M$. A tablet formulation is given. Antitumor agents Human (preparation of thiophenedicarboxamides and related compds. as histone deacetylase (HDAC) inhibitors) Neoplasm (treatment; preparation of thiophenedicarboxamides and related compds. as histone deacetylase (HDAC) inhibitors) 487002-77-7P 487002-78-8P 487002-79-9P 487002-80-2P 487002-81-3P 487002-82-4P 487002-83-5P 487002-84-6P 487002-85-7P 487002-86-8P 487002-87-9P 487002-88-0P 487002-89-1P 487002-90-4P 487002-91-5P 487002-92-6P 487002-93-7P 487002-94-8P 487002-95-9P 487002-96-0P 487002-98-2P 487003-00-9P 487003-04-3P 487003-02-1P 487003-05-4P 487003-07-6P 487003-09-8P 487003-11-2P · 487003-13-4P 487003-15-6P 487003-17-8P 487003-19-0P 487003-21-4P 487003-23-6P 487003-25-8P 487003-26-9P 487003-28-1P 487003-30-5P 487003-32-7P 487003-34-9P 487003-36-1P 487003-37-2P 487003-38-3P 487003-39-4P 487003-40-7P 487003-41-8P 487003-42-9P 487003-43-0P 487003-44-1P 487003-45-2P 487003-46-3P 487003-47-4P 487003-48-5P 487003-49-6P 487003-50-9P 487003-52-1P 487003-51-0P 487003-53-2P 487003-54-3P 487003-55-4P 487003-56-5P 487003-57-6P 487003-58-7P 487003-59-8P 487003-60-1P 487003-61-2P 487003-62-3P 487003-63-4P 487003-64-5P 487003-65-6P 487003-66-7P 487003-67-8P 487003-68-9P 487003-69-0P 487003-70-3P 487003-71-4P 487003-72-5P 487003-73-6P 487003-74-7P 487003-75-8P 487003-76-9P 487003-77-0P 487003-78-1P 487003-79-2P 487003-80-5P 487003-81-6P 487003-82-7P 487003-83-8P 487003-84-9P 487003-85-0P 487003-86-1P 487003-87-2P 487003-88-3P 487003-89-4P 487003-90-7P 487003-91-8P 487003-92-9P 487003-94-1P 487003-93-0P 487003-95-2P 487003-96-3P 487003-97-4P 487003-98-5P 487003-99-6P 487004-00-2P 487004-01-3P 487004-02-4P 487004-03-5P 487004-04-6P 487004-05-7P 487004-06-8P 487004-07-9P 487004-08-0P 487004-09-1P 487004-10-4P 487004-11-5P 487004-12-6P 487004-13-7P 487004-14-8P 487004-15-9P 487004-16-0P 487004-17-1P 487004-18-2P 487004-19-3P 487004-20-6P

487004-91-1P 487004-92-2P 487004-93-3P 487004-95-5P 487004-97-7P 487010-28-6P RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES

487004-23-9P

487004-28-4P

487004-33-1P

487004-38-6P

487004-43-3P

487004-48-8P

487004-57-9P

487004-62-6P

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487004-75-1P

487004-84-2P

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487004-24-0P

487004-29-5P

487004-34-2P

487004-39-7P

487004-44-4P

487004-49-9P

487004-58-0P

487004-64-8P

487004-68-2P

487004-77-3P

487004-86-4P

487004-25-1P

487004-30-8P

487004-35-3P

487004-40-0P

487004-45-5P

487004-50-2P

487004-59-1P

487004-79-5P

487004-88-6P

(claimed compound; preparation of thiophenedicarboxamides and related compds.

as histone deacetylase (HDAC) inhibitors)

487004-22-8P

487004-27-3P

487004-32-0P

487004-37-5P

487004-42-2P

487004-47-7P

487004-56-8P

487004-61-5P

487004-66-0P

487004-73-9P

487004-82-0P

487004-90-0P

ΙT 9076-57-7, Histone deacetylase

487004-21-7P

487004-26-2P

487004-31-9P

487004-36-4P

487004-41-1P

487004-46-6P

487004-51-3P

487004-55-7P

487004-60-4P

487004-65-9P

487004-71-7P

487004-81-9P

487004-89-7P

IT

IT

ΙT

RL: BSU (Biological study, unclassified); BIOL (Biological study) (inhibitors; preparation of thiophenedicarboxamides and related compds. as histone deacetylase (HDAC) inhibitors)

IT 100-21-0, Terephthalic acid, reactions 118-31-0, 1Aminomethylnaphthalene 622-33-3, O-Benzylhydroxylamine 3858-80-8,
3,5-Dimethylbenzylamine 4152-90-3, 3-Chlorobenzylamine 18469-52-8,
Methyl 4-aminomethylbenzoate 50340-79-9, Thiophene-2,5-dicarboxylic acid
monomethyl ester 487005-05-0

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of thiophenedicarboxamides and related compds. as histone deacetylase (HDAC) inhibitors)

IT 487004-98-8P 487004-99-9P 487005-01-6P 487005-02-7P 487005-07-2P RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of thiophenedicarboxamides and related compds. as histone deacetylase (HDAC) inhibitors)

RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

- L8 ANSWER 6 OF 12 CAPLUS COPYRIGHT 2007 ACS on STN
- TI Preparation of N-acylaminoalkanehydroxamic acids as IL-6 production inhibitors
- AN 2002:736103 CAPLUS
- DN 137:247516
- TI Preparation of N-acylaminoalkanehydroxamic acids as IL-6 production inhibitors
- IN Naka, Masao; Takahashi, Kanji
- PA Ono Pharmaceutical Co., Ltd., Japan
- SO PCT Int. Appl., 194 pp.
- CODEN: PIXXD2
- DT Patent
- LA Japanese

FAN.CNT 1

| | PATENT NO. | | | | | D | DATE | | | APPL | ICAT | ION | NO. | | D | ATE | |
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| | | | | | | | | | | JP 2 | 001- | 8130. | 2 | ž | A 2 | 0010 | 321 |
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OS MARPAT 137:247516

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AB Interleukin 6 (IL-6) production inhibitors containing as the active ingredient hydroxamic acid derivs. (I) or equivalent thereto, non-toxic salts thereof or prodrugs of the same [R1 = C1-8 alkyl, C2-8 alkenyl or alkynyl, halo, NO2, cyano, CF3, CF3O, OR2, SR2, NR3R4, keto, cyclic group, COR5, SO2R10,

SOR10, etc. (wherein R2-R4 = H, C1-8 alkyl, C2-9 acyl, cyclic group; R5 = HO, C1-8 alkyl or alkoxy, optionally substituted NH2, cyclic group; R10 = C1-8 alkyl, cyclic group); A = single bond, C3-15 mono-, di-, or tricyclic carbocyclic ring, 5- to 18-membered mono, di-, or tricyclic heterocyclic ring containing 1-4 N, 1-2 O and/or 1-2 S atoms; E = a single bond, C1-8 alkylene, C2-8 alkenylene or alkynylene, O, SO2NH, NHSO2, CONH, NHCO, etc.; B = s single bond, C5-15 mono-, di-, or tricyclic carbocyclic ring; 5- to 18-membered mono-, di-, or tricyclic heterocyclic ring containing 1-4 N, 1-2 O and/or 1-2 S atoms; R8 = C1-8 alkyl or alkoxy, halo, NO2, cyano, CF3, CF30, HO, C1-8 hydroxyalkyl; when E is a single bond, R1 and R8 together represents a C1-4 alkylene; n = an integer of 1-5; G = a single bond, (un) substituted NHCO or CONH, O, S, SO, SO2, (un) substituted SO2NH, CO, etc.; L = C1-8 alkylene, C2-8 alkenylene or alkynylene, C2-8 alkenylene-C2-8 alkynylene, C2-8 alkylene-C2-8 alkenylene, etc.; Q = (un) substituted CONHOH, oxiranylcarbonyl, (un) substituted SH, P(O) (OH) 2 or its C1-4 alkyl ester; some proviso are given] are claimed. Because of having an IL-6 production inhibitory activity, the compds. of the general formula I are useful as preventives and/or remedies for various inflammatory diseases, sepsis, multiple myeloma, plasmacytoid leukemia, osteoporosis, cachexia, psoriasis, nephritis, kidney cell cancer, Kaposi's sarcoma, rheumatoid arthritis, hypergamma globulinemia, Castleman's disease, intra-atrial myxoma, diabetes, autoimmune diseases, hepatitis, colitis, graft-vs.-host disease, infections, endometriosis and solid cancer. The solid cancer include brain tumor, head and neck cancer, thyroid gland cancer, esophageal cancer, stomach cancer, colorectal cancer (colon cancer and rectum cancer), liver cancer, gallbladder cancer, bile duct cancer (cholangioma), pancreatic cancer, lung cancer, breast cancer, cervical cancer, uterine cancer, ovarian cancer, prostatic cancer, testicular tumor, bladder cancer, renal pelvis tumor, ureteral tumor, adrenal cancer (hypernephroma), neuroma, glioma, bone tumor, rhabdomyosarcoma, osteosarcoma, soft tissue tumor, eosinophilic granuloma, malignant melanoma, skin cancer, Wilms's tumor, etc. Thus, to a solution of 2.24 g 6-[(4-phenylbenzoyl)amino]hexanoic acid in 42 mL DMF were successively added 1-hydroxybenzotriazole hydrate 1.65, Et3N 2.91, 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride 2.07, and N-(1-methyl-1-methoxyethoxy) amine 1.14 g and stirred at room temperature for 4

to give 1.79 g N-(1-methyl-1-methoxyethoxy)-6-[(4-phenylbenzoyl)amino]hexanamide which (1.78 g) was dissolved in 4.5 m MeOH and stirred with 4.5 mL 2 N aqueous HCl at room temperature to give N-hydroxy-6-[(4-phenylbenzoyl)amino]hexanamide (II). II in vitro inhibited the production of IL-6 in human lung epithelial cell A549 with IC50 of 0.18 μ M. A tablet and an ampule formulation containing II were prepared Lymph node, disease

(Castleman's; preparation of N-acylaminoalkanehydroxamic acids as IL-6 production inhibitors as preventives and/or remedies for diseases)
Sarcoma

(Kaposi's; preparation of N-acylaminoalkanehydroxamic acids as IL-6 production

inhibitors as preventives and/or remedies for diseases)

IT Kidney, neoplasm

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(Wilms'; preparation of N-acylaminoalkanehydroxamic acids as IL-6 production inhibitors as preventives and/or remedies for diseases)

IT Uterus, neoplasm

(cervix; preparation of N-acylaminoalkanehydroxamic acids as IL-6 production inhibitors as preventives and/or remedies for diseases)

IT Bile duct, neoplasm

(cholangioma; preparation of N-acylaminoalkanehydroxamic acids as IL-6 production inhibitors as preventives and/or remedies for diseases)

IT Inflammation

Intestine, disease

(colitis; preparation of N-acylaminoalkanehydroxamic acids as IL-6 production

inhibitors as preventives and/or remedies for diseases) ΙT Intestine, neoplasm (colon; preparation of N-acylaminoalkanehydroxamic acids as IL-6 production inhibitors as preventives and/or remedies for diseases) IT Intestine, neoplasm (colorectal; preparation of N-acylaminoalkanehydroxamic acids as IL-6 production inhibitors as preventives and/or remedies for diseases) TΤ Uterus, disease (endometriosis; preparation of N-acylaminoalkanehydroxamic acids as IL-6production inhibitors as preventives and/or remedies for diseases) ΙT (eosinophilic; preparation of N-acylaminoalkanehydroxamic acids as IL-6 production inhibitors as preventives and/or remedies for diseases) Transplant and Transplantation IT (graft-vs.-host reaction; preparation of N-acylaminoalkanehydroxamic acids as IL-6 production inhibitors as preventives and/or remedies for diseases) IT Neoplasm (head and neck, head and neck; preparation of N-acylaminoalkanehydroxamic acids as IL-6 production inhibitors as preventives and/or remedies for diseases) IT Head and Neck, neoplasm (head and neck; preparation of N-acylaminoalkanehydroxamic acids as IL-6 production inhibitors as preventives and/or remedies for diseases) IT Heart, disease (intra-atrial myxoma; preparation of N-acylaminoalkanehydroxamic acids as IL-6 production inhibitors as preventives and/or remedies for diseases) ΙT Inflammation Kidney, disease (nephritis; preparation of N-acylaminoalkanehydroxamic acids as IL-6 production inhibitors as preventives and/or remedies for diseases) IT Nerve, neoplasm (neuroma; preparation of N-acylaminoalkanehydroxamic acids as IL-6 production inhibitors as preventives and/or remedies for diseases) IT Bone, neoplasm Sarcoma (osteosarcoma; preparation of N-acylaminoalkanehydroxamic acids as IL-6 production inhibitors as preventives and/or remedies for diseases) ΙT Kidney (pelvis, tumor; preparation of N-acylaminoalkanehydroxamic acids as IL-6 production inhibitors as preventives and/or remedies for diseases) Anti-infective agents IT Anti-inflammatory agents Antiarthritics Antidiabetic agents Antitumor agents Autoimmune disease Bladder, neoplasm Bone, neoplasm Brain, neoplasm Cachexia Diabetes mellitus Esophagus, neoplasm Gallbladder, neoplasm Hepatitis Human Immunomodulators Infection Inflammation

Kidney, neoplasm Liver, neoplasm

Mammary gland, neoplasm Melanoma Multiple myeloma Neuroglia, neoplasm Osteoporosis Ovary, neoplasm Pancreas, neoplasm Plasma cell leukemia Prostate gland, neoplasm Psoriasis Rheumatoid arthritis Sepsis Skin, neoplasm Stomach, neoplasm Testis, neoplasm Thyroid gland, neoplasm Urinary system, neoplasm Uterus, neoplasm (preparation of N-acylaminoalkanehydroxamic acids as IL-6 production inhibitors as preventives and/or remedies for diseases) IT Interleukin 6 RL: BSU (Biological study, unclassified); BIOL (Biological study) (preparation of N-acylaminoalkanehydroxamic acids as IL-6 production inhibitors as preventives and/or remedies for diseases) IT Kidney, neoplasm (renal cell carcinoma; preparation of N-acylaminoalkanehydroxamic acids as IL-6 production inhibitors as preventives and/or remedies for diseases) IT Carcinoma (renal cell; preparation of N-acylaminoalkanehydroxamic acids as IL-6 production inhibitors as preventives and/or remedies for diseases) ΙT Sarcoma (rhabdomyosarcoma; preparation of N-acylaminoalkanehydroxamic acids as IL-6production inhibitors as preventives and/or remedies for diseases) ΙT Animal tissue, disease (soft, neoplasm; preparation of N-acylaminoalkanehydroxamic acids as IL-6 production inhibitors as preventives and/or remedies for diseases) ΙT Neoplasm (soft-tissue; preparation of N-acylaminoalkanehydroxamic acids as IL-6 production inhibitors as preventives and/or remedies for diseases) Neoplasm (solid; preparation of N-acylaminoalkanehydroxamic acids as IL-6 production inhibitors as preventives and/or remedies for diseases) Globulins, biological studies IT RL: BSU (Biological study, unclassified); BIOL (Biological study) (γ -, hypergammaglobulinemia; preparation of Nacylaminoalkanehydroxamic acids as IL-6 production inhibitors as preventives and/or remedies for diseases) IT 461404-43-3P 461405-85-6P 461405-86-7P 461405-87-8P 461405-96-9P 461406-11-1P 461406-03-1P 461406-13-3P 461406-15-5P RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses) (preparation of N-acylaminoalkanehydroxamic acids as IL-6 production inhibitors as preventives and/or remedies for diseases) TΤ 85594-22-5P 91489-66-6P 114767-55-4P, y 151720-43-3P 174664-71-2P 190911-86-5P 190911-87-6P 191228-04-3P 223466-35-1P 251456-78-7P 408349-39-3P 461404-45-5P 461404-46-6P 461404-47-7P 461404-48-8P 461404-49-9P 461404-50-2P 461404-51-3P 461404-52-4P 461404-53-5P

Lung, neoplasm

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    RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
     (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
        (preparation of N-acylaminoalkanehydroxamic acids as IL-6 production
inhibitors
        as preventives and/or remedies for diseases)
     60-32-2, 6-Aminohexanoic acid 74-88-4, Methyl iodide, reactions
     98-59-9, p-Toluenesulfonyl chloride 107-30-2, Methoxymethyl chloride
     302-01-2, Hydrazine, reactions 644-08-6
                                                 762-04-9, Diethyl phosphonate
                1826-67-1, Vinylmagnesium bromide
                                                     2051-62-9,
                        5205-39-0
     4-Chlorobiphenyl
                                  6638-79-5, N-Methoxy-N-methylamine
                     7664-41-7, Ammonia, reactions 10387-40-3, Potassium
    hydrochloride
                  14002-51-8, 4-Phenylbenzoyl chloride 18162-48-6,
    thioacetate
    tert-Butyldimethylsilyl chloride 35444-44-1, Methyladipoyl chloride
     331230-79-6
                  461404-44-4
    RL: RCT (Reactant); RACT (Reactant or reagent)
        (preparation of N-acylaminoalkanehydroxamic acids as IL-6 production
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inhibitors as preventives and/or remedies for diseases)

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TT 91323-46-5P 251456-79-8P 331230-81-0P 331231-44-8P 461405-91-4P 461405-92-5P 461405-93-6P 461405-94-7P 461405-95-8P 461405-98-1P 461406-01-9P 461405-99-2P 461406-02-0P 461406-08-6P 461406-09-7P RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of N-acylaminoalkanehydroxamic acids as IL-6 production inhibitors

- as preventives and/or remedies for diseases)
- RE.CNT 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT
- L8 ANSWER 7 OF 12 CAPLUS COPYRIGHT 2007 ACS on STN
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| | | | | US | 2000-208688P | P | 20000601 |
| | | | | US | 2000-645430 | A 1 | 20000824 |
| AU | 2005205805 | A1 | 20050929 | AU | 2005-205805 | | 20050902 |
| | | | | ΑU | 2000-69327 | А3 | 20000824 |
| US | 2006241129 | A1 | 20061026 | US | 2006-474043 | | 20060622 |
| | | | | US | 1999-152755P | P | 19990908 |
| | | | | US | 2000-208688P | P | 20000601 |
| | | | | US | 2000-645430 | A1 | 20000824 |
| | | | | US | 2002-281875 | A3 | 20021025 |
| US | 2007010536 | A1 | 20070111 | US | 2006-473839 | | 20060622 |
| | | | | US | 1999-152755P | P | 19990908 |
| | | | | US | 2000-208688P | Р | 20000601 |
| | | | | US | 2000-645430 | A1 | 20000824 |
| | | | | US | 2002-281875 | А3 | 20021025 |
| US | 2007010669 | A1 | 20070111 | US | 2006-474042 | | 20060622 |
| | • | | | US | 1999-152755P | P | 19990908 |
| | | | | US | 2000-208688P | P | 20000601 |
| | | | | US | 2000-645430 | A 1 | 20000824 |
| | | | | US | 2002-281875 | Α1 | 20021025 |

OS MARPAT 134:237397

The present invention provides the compound having formula AB R1NHCOCH(AR2)(CH2)nCONHOH (wherein each of R1 and R2 is, substituted or unsubstituted, aryl, cycloalkyl, cycloalkylamino, naphtha, pyridineamino, piperidino, tert-Bu, aryloxy, arylalkyloxy, or pyridine group; wherein A is an amido moiety, O, S, NH, or CH2; and wherein n is an integer from 3 The present invention also provides a method of selectively inducing growth arrest, terminal differentiation and/or apoptosis of neoplastic cells and thereby inhibiting proliferation of such cells. Moreover, the present invention provides a method of treating a patient having a tumor characterized by proliferation of neoplastic cells. Lastly, the present invention provides a pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically acceptable amount of the compound above. Thus, N-benzoyl-L- α -aminosuberateanilide, i.e. PhCO-Asu-NHPh, was condensed with tert-butyldiphenylsilyloxyamine using 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride in CH2Cl2 at room temperature for 12 h, followed by deprotection with 5% CF3CO2H in

CH2Cl2 for 1.5 h to give PhCO-Asu(NHOH)-NHPh (I). I and PhCH2O2C-Asu(NHOH)-NHR (R = quinolin-8-yl) showed activity of murine erythroleukemia cell (MEL) differentiation at 200 and 40 nM, resp., and inhibited histone deacetylase (HDAC) with ID50 of 1 and <10 nM, resp. Apoptosis

(neoplastic cells; preparation of alkanoic acid derivs. as novel class of cytodifferentiating agents and histone deacetylase inhibitors)

IT Antitumor agents
Cell differentiation

IT

(preparation of alkanoic acid derivs. as novel class of cytodifferentiating agents and histone deacetylase inhibitors)

IT Fatty acids, preparation

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of alkanoic acid derivs. as novel class of cytodifferentiating agents and histone deacetylase inhibitors)

| T.L. | /661-21-4P | 14964/-/8-9P | 149647-93-8P | 149648-28-2P | 329966-64-5P |
|------|-----------------------|--------------|-----------------------|--------------|--------------|
| | 329966-65-6P | 329966-66-7P | 329966-67-8P | 329966-68-9P | 329966-69-0P |
| | 329966-70-3P | 329966-71-4P | 329966-72-5P | 329966-73-6P | 329966-74-7P |
| | 329966-75 - 8P | 329966-76-9P | 329966-77 - 0P | 329966-78-1P | 329966-79-2P |
| | 329966-80-5P | 329966-81-6P | 329966-82-7P | 329966-83-8P | 329966-84-9P |

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329966-86-1P 329966-87-2P 329966-88-3P
     329966-85-0P
                                   329966-91-8P
     329966-89-4P
                    329966-90-7P
                                                   329966-92-9P
                                                                  329966-93-0P
     329966-97-4P
                                                   329967-01-3P
                    329966-98-5P
                                   329967-00-2P
                                                                  329967-02-4P
     329967-03-5P
                    329967-19-3P 329967-25-1P
                                                   329967-32-0P
                                                                  329967-33-1P
                    329967-35-3P
     329967-34-2P
                                   329967-36-4P
                                                   329967-37-5P
                                                                  329967-38-6P
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);
     BIOL (Biological study); PREP (Preparation); USES (Uses)
        (preparation of alkanoic acid derivs. as novel class of cytodifferentiating
        agents and histone deacetylase inhibitors)
     9076-57-7, Histone deacetylase
IT
     RL: BPR (Biological process); BSU (Biological study, unclassified); MSC
     (Miscellaneous); BIOL (Biological study); PROC (Process)
        (preparation of alkanoic acid derivs. as novel class of cytodifferentiating
        agents and histone deacetylase inhibitors)
IT
     60-32-2, 6-Aminohexanoic acid 62-53-3, Aniline, reactions 65-85-0,
     Benzoic acid, reactions
                              100-61-8, N-Methylaniline, reactions
                                                                       124-63-0,
     Methanesulfonyl chloride 407-25-0, Trifluoroacetic anhydride
                                                                       541-16-2.
     Di-tert-butyl malonate 578-66-5, 8-Aminoquinoline 591-80-0,
     4-Pentenoic acid 813-77-4, Dimethyl chlorophosphate
                                                              3946-32-5, Suberic
     acid monomethyl ester 10387-40-3, Potassium thioacetate
                                                                 22809-37-6,
     6-Bromohexanoyl chloride 49616-61-7, Methyl 6-bromo-2,4-hexadienoate 49645-27-4 103587-51-5, tert-Butyldiphenylsilyloxyamine
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (preparation of alkanoic acid derivs. as novel class of cytodifferentiating
        agents and histone deacetylase inhibitors)
IT
     6404-29-1P, 6-(tert-Butoxycarbonylamino)hexanoic acid
                                                              41624-92-4P
     56911-48-9P
                   58804-62-9P
                                 70374-95-7P
                                               105612-01-9P
                                                              174784-94-2P
     329966-94-1P
                    329966-95-2P
                                   329966-96-3P
                                                  329966-99-6P
                                                                  329967-04-6P
                    329967-06-8P
     329967-05-7P
                                   329967-07-9P
                                                  329967-08-0P
                                                                  329967-09-1P
     329967-10-4P
                    329967-11-5P
                                   329967-12-6P
                                                  329967-13-7P
                                                                  329967-14-8P
     329967-15-9P
                    329967-17-1P
                                   329967-18-2P
                                                  329967-20-6P
                                                                  329967-21-7P
     329967-22-8P
                    329967-23-9P
                                   329967-24-0P
                                                  329967-26-2P
                                                                  329967-27-3P
     329967-28-4P
                    329967-29-5P
                                   329967-30-8P
                                                  329967-31-9P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (preparation of alkanoic acid derivs. as novel class of cytodifferentiating
        agents and histone deacetylase inhibitors)
     ANSWER 8 OF 12 CAPLUS COPYRIGHT 2007 ACS on STN
ΤI
     Preparation of hydroxamic acids and their use as antitumor agents
AN
     1998:430728 CAPLUS
DN
     129:148826
     Preparation of hydroxamic acids and their use as antitumor agents
TI
     Suzuki, Tsuneji; Tsuchiya, Katsutoshi; Saito, Akiko; Yamashita, Satoshi
IN
     Mitsui Petrochemical Industries, Ltd., Japan
PA
SO
     Jpn. Kokai Tokkyo Koho, 20 pp.
     CODEN: JKXXAF
DT
     Patent
LΑ
     Japanese
FAN.CNT 1
     PATENT NO.
                         KIND
                                DATE
                                            APPLICATION NO.
                                                                   DATE
PΙ
     JP 10182583
                                19980707
                         Α
                                            JP 1996-345797
                                                                   19961225
                                            JP 1996-345797
os
    MARPAT 129:148826
GI
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$$\mathbb{R}^2$$
 ACONHOH \mathbb{R}^2 \mathbb{R}^2

AB Hydroxamic acids I [A = CH2CH2, CH:CH, C.tplbond.C; R1, R2 = H, NH2, NO2, OH, halo, C1-4 alkyl, C1-4 alkoxy, C1-4 (di)alkylamino, C1-4 alkylthio; Z = bond, CO, NHCO, CH2; the bond A is at meta or para position against the terminal benzene ring] and their pharmacol. acceptable salts are prepared Amidation of 3-[4-(N,N-dimethyl)amino]benzoylcinnamic acid with H2NOH.HCl gave the corresponding hydroxamic acid with 14% yield, which at 1 μM induced differentiation of A2780 cell.

IT Cell differentiation

4-Phenylcinnamic acid

(inducers; preparation of hydroxamic acids as antitumor agents)

IT Antitumor agents

(preparation of hydroxamic acids as antitumor agents)

IT 191228-41-8P 210705-43-4P 210705-44-5P 210705-45-6P 210705-46-7P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of hydroxamic acids as antitumor agents)

IT 210705-56-9

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(preparation of hydroxamic acids as antitumor agents)

IT 88-74-4, 2-Nitroaniline 98-88-4, Benzoyl chloride 107-21-1, 1,2-Ethanediol, reactions 619-66-9, Terephthalaldehydic acid 619-84-1 1099-45-2 1122-91-4, 4-Bromobenzaldehyde 3132-99-8, 3-Bromobenzaldehyde 5470-11-1, Hydroxylamine hydrochloride 13026-23-8,

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of hydroxamic acids as antitumor agents)

IT 10602-01-4P, 2-(4-Bromophenyl)-1,3-dioxolane 17789-14-9P, 2-(3-Bromophenyl)-1,3-dioxolane 71856-95-6P, 3-Benzoylbenzaldehyde 96251-93-3P 209784-99-6P 210705-47-8P 210705-48-9P 210705-49-0P 210705-50-3P 210705-51-4P 210705-52-5P 210705-53-6P 210705-54-7P 210705-55-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of hydroxamic acids as antitumor agents)

- L8 ANSWER 9 OF 12 CAPLUS COPYRIGHT 2007 ACS on STN
- TI Preparation of arylhydroxamates and related compounds as potent inducers of terminal differentiation.
- AN 1998:8261 CAPLUS
- DN 128:75197
- TI Preparation of arylhydroxamates and related compounds as potent inducers of terminal differentiation.
- IN Breslow, Ronald; Marks, Paul A.; Rifkind, Richard A.
- PA Sloan-Kettering Institute for Cancer Research, USA
- SO U.S., 24 pp., Cont.-in-part of U.S. 5,369,108. CODEN: USXXAM
- DT Patent
- LA English
- FAN.CNT 3

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----|------------|------|----------|-----------------|----------|
| | | | | | |
| PΙ | US 5700811 | Α | 19971223 | US 1994-246363 | 19940519 |

| | | 5060100 | | | | | | | | | | -771760 | | A2 | 19911004 | |
|------|-------|-----------|------|------|------------|---------|-------|------|----------|-----|--------|-----------|-------|------|----------------------|----|
| | | 5369108 | | | Α | | 1994 | | | | | -771760 | | | 19911004 | |
| | AT | 183185 | | | T | | 1999 | 0815 | | | | -922033 | | | 19921005 | |
| | | 0104015 | | | | | | • | | | | -771760 | | Α | 19911004 | |
| | ES | 2134815 | | | Т3 | | 1999 | 1016 | | | | -922033 | | | 19921005 | |
| | | 0000000 | | | | | | | | | | -771760 | | Α | 19911004 | |
| | JP | 20032266 | 80 | | Α | | 2003 | 0812 | | | | -337049 | | | 19921005 | |
| | | | | | | | | | U | JS | 1991- | -771760 | | | 19911004 | |
| | | 5000616 | | | _ | | | | | | | -507109 | | A3 | 19921005 | |
| | US | 5932616 | | | Α | | 1999 | 0803 | | | | -222685 | | | 19940404 | |
| | | 0100065 | | | | | | | | | | -771760 | | A3 | 19911004 | |
| | CA | 2190765 | | | A1 | | 1995 | 1130 | | | | -2190765 | i | | 19950519 | |
| | F-7-0 | 0501077 | | | | | | | | | | -246363 | | | 19940519 | |
| | WO | 9531977 | | | A1 | | 1995 | 1130 | · W | Ю | 1995- | -US6554 | | | 19950519 | |
| | | W: AU, | | | | | | | | | | | | | _ | |
| | | RW: AT, | BE, | CH, | DE, | DK, | , ES, | FR, | GB, | GF | ?, IE, | IT, LU | , MC | , N | L, PT, SE | |
| | זזא | 9526474 | | | _ | | 1005 | 1010 | | | | | | | 19940519 | |
| | | 692561 | | ٠ | A | | 1995 | | | W | 1995- | -26474 | | | 19950519. | |
| | ΑU | 092361 | | | В2 | | 1998 | 0611 | | . ~ | 1004 | 0.4.60.60 | | _ | | |
| | | | | | | | | | | | | | | | 19940519 | |
| | מים | 760657 | | | 2.1 | | 1007 | 0010 | | | | -US6554 | | W | 19950519 | |
| | | 760657 | | | A1 | | 1997 | | | P | 1995- | -921378 | | | 19950519 | |
| | LF | | DE | CH | B1 | | 2003 | | | c n | | TM T T | | | | |
| | | K. AI, | DE, | Cn, | υE, | אמ | , ES, | rK, | GB, | GK | 1004 | 1T, LI | , FO | , M | C, NL, PT, | SE |
| | | | | | | | | | U
147 | 0 | 1994- | ·US6554 | | | 19940519 | |
| | ΔТ | 253906 | | | d. | | 2003 | 1115 | 7\ | m- | 1005 | 921378 | | | 19950519
19950519 | |
| | 111 | 233300 | | | 1 | | 2003 | 1110 | | | | 246363 | | | | |
| | | | | | | | | | | | | ·US6554 | | | 19940519
19950519 | |
| | ES | 2210293 | | | Т3 | | 2004 | 0701 | | | | 921378 | | W | 19950519 | |
| | | 2210233 | | | . 13 | | 2004 | 0,01 | | | | 246363 | | 7 | 19930519 | |
| | ΑU | 9662063 | | | Α | | 1996 | 1017 | | | | 62063 | | A | 19960813 | |
| | | 708115 | | | B2 | | 1999 | | | .0 | 1990- | 02003 | | | 19960613 | |
| | | | | | 22 | | 1000 | 0,25 | 11 | S | 1991_ | 771760 | | Δ | 19911004 | |
| | US | 6087367 | | | Α | | 2000 | 0711 | | | | 314195 | | | 19990518 | |
| | | | | | •• | | 2000 | 0,11 | | | | 771760 | | | 19911004 | |
| | | | | | | | | | | | | 222685 | | | 19940404 | |
| | US | 38506 | | | E1 | | 2004 | 0420 | | | 2001- | | | 111 | 20011102 | |
| | | | | | | | | | | | | 771760 | | A5 | 19911004 | |
| PATE | NT E | FAMILY IN | FORM | ATIO | V: | | | | | | | | | - 10 | 13311001 | |
| FAN | 199 | 3:538765 | | | | | | | | | | | | | | |
| | PAT | ENT NO. | | | KINI |) | DATE | | A | PP | LICAT | ION NO. | | | DATE | |
| | | | | | | - | | | _ | | | | | - | | |
| PI | WO | 9307148 | | | A1 | | 1993 | 0415 | W | 0 | 1992- | US8454 | | | 19921005 | |
| | | W: AU, | | | | | | | | | | | | | | |
| | | RW: AT, | BE, | CH, | DE, | DK, | ES, | FR, | GB, | GR | , IE, | IT, LU | , MC, | NI | L, SE | |
| | | | | | | | | | ប | S | 1991- | 771760 | | | 19911004 | |
| | | 5369108 | | | Α | | 1994 | 1129 | | | | 771760 | | | 19911004 | |
| | | 9228703 | | | Α | | 19930 | 0503 | A | U | 1992- | 28703 | | | 19921005 | |
| | AU | 668696 | | | B2 | | 19960 | 0516 | | | | | | | | |
| | | | | | | | | | U | S | 1991- | 771760 | | Α | 19911004 | |
| | | | | | | | | | W | 0 | 1992- | US8454 | | Α | 19921005 | |
| | | 642509 | | | A 1 | | 19950 | | E | P | 1992- | 922033 | | | 19921005 | |
| | EP | 642509 | | | В1 | | 19990 | | | | | | | | | |
| | | R: AT, | BE, | CH, | DE, | DK, | ES, | FR, | | | | | , ĻU, | MC | C, NL, SE | |
| | | | | | | | | | | | | 771760 | | | 19911004 | |
| | | | | | | | | | | | | US8454 | | W | 19921005 | |
| | | 07502494 | | | T | | 19950 | | J | P | 1993- | 507109 | | | 19921005 | |
| | JP | 3432823 | | | B2 | | 20030 | 0804 | | | | | | | | |
| | | | | | | | | | | | | 771760 | | A | 19911004 | |
| | | 60.465 | | | | | | | | | | US8454 | | | 19921005 | |
| | | 67421 | | | A2 | | 19950 | | н | U : | 1994- | 959 | | | 19921005 | |
| | HU | 225497 | | | B 1 | | 20070 | 0129 | | | | | | | | |
| | | | | | | | | | | | | | | | | |

| | | | | US 1991-771760 | A 19911004 |
|-----|-----------------|-------------|-----------|----------------------------------|-------------------|
| | | | | WO 1992-US8454 | W 19921005 |
| | RU 2128643 | C1 | 19990410 | RU 1994-21660 | 19921005 |
| | | | | US 1991-771760 | A 19911004 |
| | | | | WO 1992-US8454 | W 19921005 |
| | AT 183185 | T | 19990815 | AT 1992-922033 | 19921005 |
| | | | | US 1991-771760 | A 19911004 |
| | ES 2134815 | Т3 | 19991016 | ES 1992-922033 | 19921005 |
| | | | | US 1991-771760 | A 19911004 |
| | JP 2003226680 | Α | 20030812 | JP 2002-337049 | 19921005 |
| | | | | US 1991-771760 | A 19911004 |
| | | | | JP 1993-507109 | A3 19921005 |
| | CA 2120619 | С | 20061121 | CA 1992-2120619 | 19921005 |
| | e e | | | US 1991-771760 | A 19911004 |
| | | | | WO 1992-US8454 | W 19921005 |
| | NO 9401166 | Α | 19940530 | NO 1994-1166 | 19940329 |
| | | | | US 1991-771760 | A 19911004 |
| | | | | WO 1992-US8454 | A 19921005 |
| | FI 9401537 . | Α | 19940531 | FI 1994-1537 | 19940331 |
| | | | | US 1991-771760 | A 19911004 |
| | | | | WO 1992-US8454 | W 19921005 |
| | US 5932616 | Α | 19990803 | US 1994-222685 | 19940404 |
| | | | | US 1991-771760 | A3 19911004 |
| | AU 9662063 | Α | 19961017 | AU 1996-62063 | 19960813 |
| | AU 708115 | B2 | 19990729 | | |
| | | | | US 1991-771760 | A 19911004 |
| | US 6087367 | Α | 20000711 | US 1999-314195 | 19990518 |
| | | | | US 1991-771760 | A3 19911004 |
| | | E1 | , | | A1 19940404 |
| | US 38506 | E1 | 20040420 | US 2001-4411 | 20011102 |
| | • | | | US 1991-771760 | A5 19911004 |
| FAN | 1996:181546 | | | | |
| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
| PI | WO 9531977 | A1 | 19951130 | WO 1995-US6554 | 19950519 |
| | W: AU, CA, | | | | 13300013 |
| | RW: AT, BE, | CH, DE, DK, | , ES, FR, | GB, GR, IE, IT, LU, 1 | MC. NI. PT. SE |
| | | | | US 1994-246363 | A 19940519 |
| | US 5700811 | Α | 19971223 | US 1994-246363
US 1994-246363 | 19940519 |
| | | | | US 1991-771760 | A2 19911004 |
| | AU 9526474 | Α | 19951218 | AU 1995-26474 | 19950519 |
| | AU 692561 | B2 | 19980611 | | |
| | | | | US 1994-246363 | A 19940519 |
| | | | | WO 1995-US6554 | W 19950519 |
| | EP 760657 | A 1 | 19970312 | EP 1995-921378 | 19950519 |
| | EP 760657 | B1 | 20031112 | | 2000020 |
| | R: AT, BE, | | | GB, GR, IE, IT, LI, I | U. MC. NL. PT. SE |
| | | | | US 1994-246363 | A 19940519 |
| | | | | WO 1995-US6554 | W 19950519 |
| | AT 253906 | T | 20031115 | AT 1995-921378 | 19950519 |
| | | | | US 1994-246363 | A 19940519 |
| | | | | WO 1995-US6554 | W 19950519 |
| os | MARPAT 128:7519 | 7 | | | |

OS MARPAT 128:75197

(inducers of terminal differentiation of neoplastic cells; preparation of

AB R1CO(CH2)nCOR2 [R1 = R2 = (substituted) arylamino, cycloalkylamino, pyridineamino, piperidino, 9-purine-6-amino, thiazoleamino; or R1 ≠ R2 and R1 = NR3R4; R3, R4 = H, OH, (substituted) alkyl, alkenyl, cycloalkyl, aryl, alkoxy, aryloxy, aralkoxy, pyridyl; R3R4N = piperidino; n = 4-8; R2 = hydroxylamino, OH, amino, alkoxy], and related compds., were prepared Thus, 3-HONHCOC6H4CH:CHCONHOH (prepared by reaction of H2NOSiMe3 with the corresponding diacid dichloride) induced terminal differentiation with an optimal concentrate of 4 μM with 73% benzidine reactive cells.

IT Cell differentiation

arylhydroxamates and related compds. as potent inducers of terminal differentiation)

IT Antitumor agents

(preparation of arylhydroxamates and related compds. as potent inducers of terminal differentiation)

5502-67-0P 39642-93-8P IT 149647-78-9P 149647-81-4P 149647-82-5P 149647-83-6P 149647-85-8P 149647-86-9P 149647-87-0P 149647-88-1P 149647-89-2P 149647-90-5P 149647-91-6P 149647-97-2P 149647-96-1P 149647-98-3P 149648-24-8P 149648-29-3P 149648-30-6P 149648-31-7P 149648-32-8P 149648-39-5P 149648-46-4P 149648-49-7P 149648-50-0P 149648-52-2P 149648-54-4P 149648-56-6P 149648-57-7P 149648-68-0P 149648-69-1P 174664-65-4P 174664-66-5P 174664-68-7P 174664-70-1P 174664-71-2P 200800-88-0P 200800-89-1P RL: BAC (Biological activity or effector, except adverse); BSU (Biological

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of arylhydroxamates and related compds. as potent inducers of terminal differentiation)

IT 60-32-2, 6-Aminocaproic acid 62-53-3, Benzenamine, reactions 98-88-4, 100-20-9, 1,4-Benzenedicarbonyl dichloride Benzoyl chloride 504-24-5, 622-33-3, O-Benzylhydroxylamine 4-Aminopyridine 929-17-9, 7-Aminoheptanoic acid 2687-43-6, O-Benzylhydroxylamine hydrochloride 3946-32-5, Suberic acid monomethyl ester 10027-07-3, Suberoyl chloride 16323-43-6, 1,4-Phenylenediacrylic acid 22737-36-6, 0-Trimethylsilylhydroxylamine

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of arylhydroxamates and related compds. as potent inducers of terminal differentiation)

IT 1149-15-1P, 7-(Benzoylamino)heptanoic acid 94136-35-3P, N-Benzyloxy-6-bromohexanamide 99647-94-6P 149648-51-1P,

N-Benzyloxy-6-cyanohexanamide 200800-91-5P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of arylhydroxamates and related compds. as potent inducers of terminal differentiation)

- L8 ANSWER 10 OF 12 CAPLUS COPYRIGHT 2007 ACS on STN
- TI Preparation of alkanedicarboxylic acid amides as novel potent inducers of terminal differentiation of neoplastic cell
- AN 1996:181546 CAPLUS
- DN 124:260602
- TI Preparation of alkanedicarboxylic acid amides as novel potent inducers of terminal differentiation of neoplastic cell
- IN Breslow, Ronald; Marks, Paul A.; Rifkind, Richard A.
- PA Sloan-Kettering Institute for Cancer Research, USA; Trustees of Columbia University in the City of New York
- SO PCT Int. Appl., 98 pp. CODEN: PIXXD2
- DT Patent
- LA English
- FAN.CNT 3

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| PI | WO 9531977
W: AU, CA, JP, | | A1
MX | 19951130 | WO 1995-US6554 | 19950519 |
| | RW: AT | r, BE, CH, | DE, DK | , ES, FR, | GB, GR, IE, IT, LU, | MC, NL, PT, SE |
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AB

Alkanedicarboxylic acid amides R1CO(CH2)nCOR2 [I; wherein each of R1 and R2 are independently the same or different from each other; R1 and R2 are the same, each is a substituted or unsubstituted arylamino, cycloalkylamino, pyridineamino, piperidino, 9-purine-6-amine, or thiazoleamino group; when R1 and R2 are different, R1 = R3-NR4, wherein each of R3 and R4 are independently the same as or different from each other and are H, HO, (un) substituted, branched or unbranched alkyl, alkenyl, cycloalkyl, aryl, alkyloxy, aryloxy, arylalkyloxy, or pyridine group, or R3 and R4 bond together to form a piperidine group and R2 is a hydroxylamino, HO, NH2, alkylamino, dialkylamino or alkyloxy group; n = aninteger from about 4-8], which inhibit proliferation of such cells and are useful for treating a patient having a tumor characterized by proliferation of neoplastic cells, are prepared Thus, chlorination of suberic acid monomethyl ester with oxalyl chloride benzene containing DMF to suberoyl chloride followed by condensation with O-benzylhydroxylamine in pyridine/CHCl3 at room temperature overnight gave 89% PhCH2ONHCO(CH2)6CO2Me. Hydrogenolysis of the latter compound in the presence of 5% Pd-C under .apprx.50 psi H atmospheric to HONHC(O)(CH2)6CO2Me followed by saponification with KOH in

HONHC(O)(CH2)6CO2H. PhonHC(O)(CH2)6C(O)NHOH at 3 μ M in vitro induced the differentiation of MELC cells and HL-60 human leukemia cells by 21 and 65%, resp. Cell differentiation ΙT Neoplasm Neoplasm inhibitors (preparation of alkanedicarboxylic acid amides as inducers of terminal differentiation of neoplastic cell and as anticancer agents) IT 5502-67-0P 20073-81-8P 39642-93-8P 56384-27-1P 136268-94-5P 149647-78-9P 149647-77-8P 149647-79-0P 149647-80-3P 149647-81-4P 149647-82-5P 149647-83-6P 149647-84-7P 149647-85-8P 149647-86-9P 149647-87-0P 149647-89-2P 149647-90-5P 149647-91-6P 149647-92-7P 149647-93-8P 149647-94-9P 149647-95-0P 149647-96-1P 149647-97-2P 149647-98-3P 149647-99-4P 149648-00-0P 149648-02-2P 149648-01-1P 149648-03-3P 149648-04-4P 149648-05-5P 149648-07-7P 149648-06-6P 149648-08-8P 149648-09-9P 149648-10-2P 149648-11-3P 149648-12-4P 149648-13-5P 149648-15-7P 149648-14-6P 149648-16-8P 149648-17-9P 149648-18-0P 149648-19-1P 149648-20-4P 149648-21-5P 149648-22-6P 149648-23-7P 149648-24-8P 149648-25-9P 149648-26-0P 149648-27-1P 149648-28-2P 149648-29-3P 149648-30-6P 149648-31-7P 149648-32-8P 149648-33-9P 149648-34-0P 149648-35-1P 149648-36-2P 149648-37-3P 149648-38-4P 149648-39-5P 149648-40-8P 149648-41-9P 149648-42-0P 149648-43-1P 149648-44-2P 149648-45-3P 149648-46-4P 149648-47-5P 149648-48-6P 149648-49-7P 149648-50-0P 149648-52-2P 149648-54-4P 149648-56-6P 149648-57-7P 149648-60-2P 149648-65-7P 149648-68-0P 149648-69-1P 174664-65-4P 174664-66-5P 174664-67-6P 174664-68-7P 174664-69-8P 174664-70-1P 174664-71-2P 174664-72-3P 174664-73-4P RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (preparation of alkanedicarboxylic acid amides as inducers of terminal differentiation of neoplastic cell and as anticancer agents) ΙT 60-32-2, 6-Aminocaproic acid 62-53-3, Aniline, reactions Benzoyl chloride 100-20-9, Terephthaloyl chloride 100-61-8, N-Methylaniline, reactions 143-33-9, Sodium cyanide 504-24-5, 506-59-2, Dimethylamine hydrochloride 4-Aminopyridine 622 - 33 - 3, O-Benzylhydroxylamine 929-17-9, 7-Aminoheptanoic acid 2687-43-6, O-Benzylhydroxylamine hydrochloride 2909-38-8, m-Chlorophenyl isocyanate 3946-32-5, Suberic acid monomethyl ester 5470-11-1, Hydroxylamine 16323-43-6, 1,4-Phenylenediacrylic acid 22737-36-6, O-(Trimethylsilyl)hydroxylamine 22809-37-6, 6-Bromohexanoyl chloride 149648-51-1, N-Benzyloxy-6-cyanohexanamide RL: RCT (Reactant); RACT (Reactant or reagent) (preparation of alkanedicarboxylic acid amides as inducers of terminal differentiation of neoplastic cell and as anticancer agents) IT 1149-15-1P, 7-Benzamidoheptanoic acid 10027-07-3P, Suberoyl chloride 94136-35-3P, N-Benzyloxy-6-bromohexanamide 149647-88-1P 174664-74-5P RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (preparation of alkanedicarboxylic acid amides as inducers of terminal differentiation of neoplastic cell and as anticancer agents) L8ANSWER 11 OF 12 CAPLUS COPYRIGHT 2007 ACS on STN ΤI Nucleophilic reactions of N-hydroxy-, methoxy-, 2,3-epoxypropoxyphthalimides 1995:237245 CAPLUS AN DN 122:239480 ΤI Nucleophilic reactions of N-hydroxy-, methoxy-, 2,3-epoxypropoxyphthalimides ΑU Ranadive, V. B.; Khadilkar, B. M.; Samant, S. D. CS Org. Chem. Res. Lab., Univ. Dep. Chem. Technol., Bombay, 400 019, India

aqueous MeOH under reflux for 2 h and acidification with concentrated HCl gave

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SO Indian Journal of Chemistry, Section B: Organic Chemistry Including Medicinal Chemistry (1994), 33B(12), 1175-7 CODEN: IJSBDB; ISSN: 0376-4699
PB Publications & Information Directorate, CSIR DT Journal
LA English
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Reaction of N-hydroxyphthalimide (I, R = OH) with equivalent amts. of aliphatic AB and aromatic primary amines gives the N-substituted phthalimides I (R =PhCH2, CH2CH2Ph, Ph, CMe3, 4-Me6H4, etc.), while with excess of these amines it gives the diamides of phthalic acid, 1,2-(RNHCO) 2C6H4 [R = CH2Ph, CH2CH2Ph, CHMe2, CH2CH2Me, CH2(CH2)2Me]. The reaction of I (R = $\frac{1}{2}$ OH) with t-Bu amine gives only the Bu monoamide of phthaloylhydroxamic acid. N-methoxyphthalimide reacts in the same manner. I (R = OH) does not condense with epichlorohydrin, but condenses with epibromohydrin to give N-(2,3-epoxypropoxy)phthalimide (II) which on reaction with equivalent amts. of aliphatic primary amines gives the N-substituted phthalimides and with excess of the amines it gives the diamides of phthalic acid. The reaction of II with aromatic primary amines gives only the N-arylphthalimides. Secondary amines do not react with II. ΙT 62-53-3, Aniline, reactions 64-04-0, 2-Phenyl-1-ethylamine 75-31-0, Isopropylamine, reactions 75-64-9, tert-Butylamine, reactions 85-44-9, Phthalic anhydride 95-53-4, 2-Methylaniline, reactions 100-46-9, 106-49-0, 4-Methylaniline, reactions Benzylamine, reactions 107-10-8, 1-Propanamine, reactions 109-73-9, 1-Butanamine, reactions 3132-64-7, Epibromhydrin RL: RCT (Reactant); RACT (Reactant or reagent) (nucleophilic reactions of N-hydroxy-, methoxy-, and (epoxypropoxy)-phthalimides) ΙT 524-38-9P, N-Hydroxyphthalimide 1914-20-1P, N-Methoxyphthalimide 58288-28-1P, 1H-Isoindole-1,3(2H)-dione, 2-hydroxy-, potassium salt 80041-90-3P RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (nucleophilic reactions of N-hydroxy-, methoxy-, and (epoxypropoxy)-phthalimides) 304-17-6P, N-Isopropylphthalimide 520-03-6P, N-Phenylphthalimide IT 1515-72-6P, N-Butylphthalimide 2141-99-3P, N-tert-Butylphthalimide 2142-01-0P, N-Benzylphthalimide 2142-03-2P, N-(p-Tolyl)phthalimide

2142-01-0P, N-Benzylphthalimide 2142-03-2P, N-(p-Tolyl)phthalimide 2464-33-7P, N-(o-Tolyl)phthalimide 5323-50-2P, N-Propylphthalimide 7501-05-5P, N-Phenethylphthalimide 19532-95-7P 19532-96-8P 38228-97-6P 38228-99-8P 38229-00-4P 162316-52-1P 162316-53-2P RL: SPN (Synthetic preparation); PREP (Preparation) (nucleophilic reactions of N-hydroxy-, methoxy-, and (epoxypropoxy)-phthalimides)

L8 ANSWER 12 OF 12 CAPLUS COPYRIGHT 2007 ACS on STN

TI Alkanedioic acid derivatives, novel potent inducers of terminal differentiation and methods of use thereof

1993:538765 CAPLUS AN

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Alkanedioic acid derivatives, novel potent inducers of terminal ΤI differentiation and methods of use thereof

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Sloan-Kettering Institute for Cancer Research, USA; Columbia University PA

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| | | | | | | | | | | US | 1994-222685 | | 19940404 |
| | US | 38506 | 5 | | | E1 | 2 | 20040 | 420 | US | 2001-4411 | | 20011102 |
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| EP 760657 EP 760657 B1 20031112 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, US 1994-246363 A 19940519 WO 1995-US6554 W | | | | | | | | | | | | | | | | |
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| US 1994-246363 A 19940519 WO 1995-US6554 W 19950519 AT 253906 T 20031115 AT 1995-921378 19950519 US 1994-246363 A 19940519 WO 1995-US6554 W 19950519 WO 1995-US6554 W 19950519 ES 2210293 T3 20040701 ES 1995-921378 19950519 US 1994-246363 A 19940519 AU 9662063 A 19961017 AU 1996-62063 19960813 AU 708115 B2 19990729 US 1991-771760 A 19911004 US 6087367 A 20000711 US 1999-314195 19990518 | | | | BE. | CH. | | | | | GR | GE | 2. TE. TO T | T . T1 | T M | יים אוו. יים | |
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| US 6087367 A 20000711 US 1999-314195 19990518 | | ΑU | ,00113 | | | BZ | | 19990 | 129 | | 110 | 1001 333360 | | _ | 10011001 | |
| 13330010 | | IIC | 6097267 | | | 78 | | 20000 | 711 | | | | | Α | | |
| US 1991-771760 A3 19911004 | | US | 000/36/ | | | Α | | 20000 | //11 | | | | | | | |
| 13 13311001 | | | | | | | | | | | US | 1991-771760 | | A3 | 19911004 | |

OS MARPAT 119:138765

AB Alkylene bisamides and monoamides R1CO(CH2)nCOR2 [R1 = R2 = (un)substituted arylamino, cycloalkylamino, pyridylamino, piperidino, 9-purine-6-amino, thiazolylamino; R1 = R3R4N, where R3 = H, OH, (un)substituted alkyl, alkenyl, cycloalkyl, aryl, alkyloxy, aryloxy, arylalkyloxy, pyridyl or R3R4N = piperidino; R2 = hydroxyamino, hydroxy, amino, alkylamino, dialkylamino, alkyloxy; n = 4-8] were prepared for selectively inducing terminal differentiation of neoplastic cells and thereby inhibiting their proliferation (data tabulated). Thus, a pyridine solution of H2NOCH2Ph, H2NOMe, and suberoyl chloride was stirred overnight at room temperature The product was treated with 10% HCl in HCCl3-MeOH and hydrogenated over 5% Pd/C to give HONHCO(CH2)6CONHOMe.

IT 67-62-9, O-Methylhydroxylamine 108-91-8, Cyclohexylamine, reactions 110-89-4, Piperidine, reactions 622-33-3, O-Benzylhydroxylamine RL: RCT (Reactant); RACT (Reactant or reagent) (acylation of, with suberic acid derivative)

IT 96-50-4, 2-Thiazolamine 455-14-1 462-08-8, 3-Aminopyridine 3544-25-0 6274-22-2, 4-Amino-N-methylbenzamide 26071-05-6, 4-Amino-N-hydroxybenzamide

RL: RCT (Reactant); RACT (Reactant or reagent)
 (acylation of, with suberic chloride)

IT 110-70-3, N,N'-Dimethylethylenediamine

RL: RCT (Reactant); RACT (Reactant or reagent)
(acylation of, with suberic chloride monomethyl ester)

IT 372-39-4, 3,5-Difluoroaniline 504-24-5, 4-Pyridinamine 782-45-6 873-74-5 1885-29-6 2237-30-1 22737-36-6, 0-(Trimethylsilyl)hydroxylamine

RL: RCT (Reactant); RACT (Reactant or reagent)
 (acylation of, with suberoyl chloride)

IT 60-32-2

RL: RCT (Reactant); RACT (Reactant or reagent) (acylation of, with terephthaloyl chloride)

IT 100-20-9, 1,4-Benzenedicarbonyl dichloride 10027-07-3, Suberoyl chloride 23713-85-1

RL: RCT (Reactant); RACT (Reactant or reagent)
 (amidation of)

IT 111-19-3, Decanedioic dichloride 111-50-2, Hexanedioic dichloride 123-98-8, Nonanedioic dichloride 142-79-0, Heptanedioic dichloride RL: RCT (Reactant); RACT (Reactant or reagent) (amidation of, with aniline or methylaniline)

IT 22809-37-6, 6-Bromohexanoyl chloride 78582-38-4, Heptanedioic chloride benzyl ester

RL: RCT (Reactant); RACT (Reactant or reagent) (amidation of, with benzylhydroxylamine)

IT 41624-92-4P, Suberic chloride methyl ester
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and amidation of)

IT 94136-35-3P, N-Benzyloxy-6-bromohexanoyl amide
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
 (Reactant or reagent)
 (preparation and cyanation of)

IT 149648-49-7P 149648-51-1P, N-Benzyloxy-6-cyanohexanoylamide 149648-53-3P

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(Reactant or reagent)
        (preparation and debenzylation of)
IT
     5502-67-0P 149647-78-9P 149647-81-4P 149647-82-5P 149647-83-6P
    149647-85-8P 149647-86-9P 149647-88-1P 149647-89-2P
                                                              149647-90-5P
     149647-91-6P
                  149647-96-1P 149647-97-2P
                                                149647-98-3P
                                                              149648-24-8P
     149648-29-3P 149648-30-6P 149648-39-5P
    RL: SPN (Synthetic preparation); PREP (Preparation)
        (preparation and terminal differentiation inducer activity of)
IT
    2409-13-4P 39642-93-8P 149648-50-0P 149648-52-2P 149648-54-4P
    149648-55-5P 149648-56-6P 149648-57-7P 149648-58-8P 149648-59-9P
    149648-60-2P
                  149648-61-3P
                                 149648-62-4P
                                               149648-63-5P
                                                              149648-64-6P
    149648-65-7P 149648-66-8P 149648-67-9P
                                              149648-68-0P
                                                              149648-69-1P
    RL: SPN (Synthetic preparation); PREP (Preparation)
        (preparation of)
IT
     56384-27-1
                 136268-94-5
                              149647-77-8
                                            149647-79-0
                                                         149647-80-3
                                                         149647-94-9
     149647-84-7
                  149647-87-0
                               149647-92-7
                                           149647-93-8
                                                         149648-02-2
    149647-95-0
                                           149648-01-1
                  149647-99-4
                               149648-00-0
                                                         149648-07-7
    149648-03-3
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    149648-18-0
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                  149648-25-9
                               149648-26-0 149648-27-1 149648-28-2
                  149648-32-8
    149648-31-7
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    149648-42-0
                  149648-43-1 149648-44-2 149648-45-3 149648-46-4
    149648-47-5
                  149648-48-6
    RL: RCT (Reactant); RACT (Reactant or reagent)
        (terminal differentiation inducer activity of)
=> logoff hold
COST IN U.S. DOLLARS
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FULL ESTIMATED COST
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DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)
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                                                            -10.92
SESSION WILL BE HELD FOR 120 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 11:29:34 ON 20 FEB 2007
Connecting via Winsock to STN
Welcome to STN International! Enter x:x
LOGINID:SSSPTA1623PAZ
PASSWORD:
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SESSION RESUMED IN FILE 'CAPLUS' AT 11:55:39 ON 20 FEB 2007
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COST IN U.S. DOLLARS
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DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE

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RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT

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ENTRY | TOTAL
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| CA SUBSCRIBER PRICE | -9.36 | -10.92 |

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chain nodes : 1 2 3 4 5 6 9 10 11 12 24 25 32 33 40 41 ring nodes : 18 19 20 21 22 23 26 27 28 29 30 31 34 35 36 37 38 39 chain bonds : $1-2 \quad 2-4 \quad 3-4 \quad 4-5 \quad 5-6 \quad 9-10 \quad 11-12 \quad 19-24 \quad 24-25 \quad 27-32 \quad 32-33 \quad 35-40 \quad 40-41$ ring bonds : 18-19 18-23 19-20 20-21 21-22 22-23 26-27 26-31 27-28 28-29 29-30 30-31 34-35 34-39 35-36 36-37 37-38 38-39 exact/norm bonds : 1-2 3-4 4-5 9-10 11-12 19-24 24-25 27-32 32-33 35-40 40-41 exact bonds : 2-4 5-6 normalized bonds : 18-19 18-23 19-20 20-21 21-22 22-23 26-27 26-31 27-28 28-29 29-30 30-31 34-35 34-39 35-36 36-37 37-38 38-39

G1: [*1-*2], [*3-*4]

G2: [*5], [*6], [*7]

Match level:

1:CLASS 2:CLASS 3:CLASS 4:CLASS 5:CLASS 6:CLASS 9:CLASS 10:CLASS 11:CLASS 12:CLASS 18:Atom 19:Atom 20:Atom 21:Atom 22:Atom 23:Atom 24:CLASS 25:Atom 26:Atom 27:Atom 28:Atom 29:Atom 30:Atom 31:Atom 32:CLASS 33:Atom 34:Atom 35:Atom 36:Atom 37:Atom 38:Atom 39:Atom 40:CLASS 41:Atom

L9 STRUCTURE UPLOADED

=> d 19

L9 HAS NO ANSWERS

L9

STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.

=> seaerch 19 sss sam
COMBINATION OF STRUCTURE AND TEXT TERMS NOT VALID
The query entered contains both search terms created by
structure-building or screen commands and text search terms. L#s
created via the STRUCTURE or SCREEN commands must be searched in the
structures files separately from text terms or profiles. The L#
answer sets from structure searches can be used in crossover searches
and can be combined with text terms.

=>

=> search 19 sss sam

SAMPLE SEARCH INITIATED 11:58:21 FILE 'REGISTRY'

SAMPLE SCREEN SEARCH COMPLETED - 5037 TO ITERATE

39.7% PROCESSED 2000 ITERATIONS

INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**

BATCH **COMPLETE**

PROJECTED ITERATIONS:

96485 TO 104995

PROJECTED ANSWERS:

39 TO 104993

5 ANSWERS

L10 5 SEA SSS SAM L9

=> d scan

L10 5 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN

IN 2-Propenamide, 3-[4-[(2-dibenzofuranylsulfonyl)amino]phenyl]-N-hydroxy-

MF C21 H16 N2 O5 S

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):5

L10 5 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN
IN 2-Propenamide, N-hydroxy-3-[3-[[[4-(trifluoromethyl)phenyl]amino]sulfonyl]
 phenyl]-, (2E)- (9CI)
MF C16 H13 F3 N2 O4 S

Double bond geometry as shown.

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L10 5 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN
IN 2-Propenamide, N-hydroxy-3-[4-[(2-thienylsulfonyl)amino]phenyl]- (9CI)
MF C13 H12 N2 O4 S2

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L10 5 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN

IN 2-Propenamide, 3-[4-[[(4-chlorophenyl)sulfonyl]amino]phenyl]-N-hydroxy-,
(2E)- (9CI)

MF C15 H13 C1 N2 O4 S

Double bond geometry as shown.

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L10 5 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN
IN Benzamide, N-hydroxy-3-methyl-2-[[[5-(2-pyridinyl)-2-thienyl]sulfonyl]amino]- (9CI)
MF C17 H15 N3 O4 S2

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

ALL ANSWERS HAVE BEEN SCANNED

=> file caplus COST IN U.S. DOLLARS SINCE FILE ENTRY SESSION FULL ESTIMATED COST 1.35 323.01 DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE TOTAL ENTRY SESSION CA SUBSCRIBER PRICE 0.00 -10.92

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L11 7 L10

=> d l11 1-7 ti fbib abs

L11 ANSWER 1 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN

- TI Novel sulfonamide derivatives as inhibitors of histone deacetylase
- AN 2005:842556 CAPLUS
- DN 143:359422
- TI Novel sulfonamide derivatives as inhibitors of histone deacetylase
- AU Finn, Paul W.; Bandara, Morwena; Butcher, Chris; Finn, Angela;
 Hollinshead, Ruth; Khan, Nagma; Law, Norman; Murthy, Sreenivasa; Romero,
 Rosario; Watkins, Clare; Andrianov, Victor; Bokaldere, Rasma M.; Dikovska,
 Klara; Gailite, Vija; Loza, Einars; Piskunova, Irina; Starchenkov, Igor;
 Vorona, Maxim; Kalvinsh, Ivars
- CS TopoTarget UK Ltd., Abingdon, OX14 4RY, UK
- SO Helvetica Chimica Acta (2005), 88(7), 1630-1657 CODEN: HCACAV; ISSN: 0018-019X
- PB Verlag Helvetica Chimica Acta
- DT Journal
- LA English
- OS CASREACT 143:359422
- AB Inhibition of the enzyme histone deacetylase (HDAC) is emerging as a novel approach to the treatment of cancer. A series of novel sulfonamide derivs. were synthesized and evaluated for their ability to inhibit human HDAC. Compds. were identified which are potent enzyme inhibitors, with IC50 values in the low nanomolar range against enzyme obtained from HeLa cell exts., and with antiproliferative effects in cell culture. Extensive characterization of the structure-activity relationships of this series identified key requirements for activity. These include the direction of the sulfonamide bond and substitution patterns on the central Ph ring. The alkyl spacer between the aromatic head group and the sulfonamide functionality also influenced the HDAC inhibitory activity. One of these compds., mll.1, also designated PXD101, has entered clin. trials for solid tumors and haematol. malignancies.
- RE.CNT 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT
- L11 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN
- TI Polymer-assisted, multi-step solution phase synthesis and biological screening of histone deacetylase inhibitors
- AN 2004:231325 CAPLUS
- DN 140:406594
- TI Polymer-assisted, multi-step solution phase synthesis and biological screening of histone deacetylase inhibitors
- AU Bapna, Akanksha; Vickerstaffe, Emma; Warrington, Brian H.; Ladlow, Mark; Fan, Tai-Ping D.; Ley, Steven V.
- CS Department of Pharmacology, University of Cambridge, Cambridge, CB2 1QJ, UK
- SO Organic & Biomolecular Chemistry (2004), 2(4), 611-620 CODEN: OBCRAK; ISSN: 1477-0520
- PB Royal Society of Chemistry
- DT Journal
- LA English
- OS CASREACT 140:406594

GI

AB The polymer-assisted solution phase synthesis (PASP) of an array of hydroxamic acids I [R1 = 4-MeC6H4, 3,4-(MeO)2C6H3, 2-thienyl, etc.; R2 = H, Me] as histone deacetylase (HDAc) inhibitors is described. HDAc inhibitors have considerable potential as new anti-proliferative agents.

Selected compds. were shown to inhibit both human endothelial cell proliferation, and the formation of tubules (neovascularization) in an in vitro model of angiogenesis.

- RE.CNT 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT
- L11 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN
- Fully automated multi-step solution phase synthesis using polymer supported reagents: preparation of histone deacetylase inhibitors. [Erratum to document cited in CA140:027645]
- AN 2003:648659 CAPLUS
- DN 141:106239
- Fully automated multi-step solution phase synthesis using polymer supported reagents: preparation of histone deacetylase inhibitors. [Erratum to document cited in CA140:027645]
- AU Vickerstaffe, Emma; Warrington, Brian H.; Ladlow, Mark; Ley, Steven V.
- CS GlaxoSmithKline Cambridge Technology Centre, University of Cambridge, Cambridge, CB2 1EW, UK
- SO Organic & Biomolecular Chemistry (2003), 1(15), 2807 CODEN: OBCRAK; ISSN: 1477-0520
- PB Royal Society of Chemistry
- DT Journal
- LA English
- AB In Reference 6, the principal author Dr. D. Delorme was omitted from the reference
- L11 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN
- TI Fully automated multi-step solution phase synthesis using polymer supported reagents: preparation of histone deacetylase inhibitors
- AN 2003:534856 CAPLUS
- DN 140:27645
- TI Fully automated multi-step solution phase synthesis using polymer supported reagents: preparation of histone deacetylase inhibitors
- AU Vickerstaffe, Emma; Warrington, Brian H.; Ladlow, Mark; Ley, Steven V.
- CS GlaxoSmithKline Cambridge Technology Centre, University of Cambridge, Cambridge, CB2 1EW, UK
- SO Organic & Biomolecular Chemistry (2003), 1(14), 2419-2422 CODEN: OBCRAK; ISSN: 1477-0520
- PB Royal Society of Chemistry
- DT Journal
- LA English
- OS CASREACT 140:27645
- AB The first fully automated multi-step polymer assisted solution phase (PASP) synthesis is described. An array of histone deacetylase (HDAc) inhibitors, 3- and 4-RSO2NR1C6H4CH:CHCONHOH [R = 4-PhC6H4, 4-MeC6H4, 4-ClC6H4; R1 = H, Me, PhCH2] was prepared by an unattended 4-5 step sequence incorporating in-line catch and release purification
- RE.CNT 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT
- L11 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN
- TI Preparation of hydroxamic acids as inhibitors of histone deacetylase
- AN 2001:396861 CAPLUS
- DN 135:5455
- TI Preparation of hydroxamic acids as inhibitors of histone deacetylase
- IN Delorme, Daniel; Ruel, Rejean; Lavoie, Rico; Thibault, Carl; Abou-khalil, Elie
- PA Methylgene, Inc., Can.
- SO PCT Int. Appl., 147 pp. CODEN: PIXXD2
- DT Patent
- LA English
- FAN.CNT 1

| | PATENT NO. | | APPLICATION NO. | DATE | | | |
|----|-----------------|-------------------|---------------------------------|---------------|--|--|--|
| PI | WO 2001038322 | Al 20010531 | WO 2000-IB1881 | 20001122 | | | |
| | W: AE, AG, AL, | | BA, BB, BG, BR, BY, BZ | | | | |
| | CR, CU, CZ, | DE, DK, DM, DZ, | EE, ES, FI, GB, GD, GE | GH. GM. HR. | | | |
| | | | KG, KP, KR, KZ, LC, LK | | | | |
| | LU, LV, MA, | MD, MG, MK, MN, | MW, MX, MZ, NO, NZ, PL | PT. RO. RU. | | | |
| | SD, SE, SG, | SI, SK, SL, TJ, | TM, TR, TT, TZ, UA, UG | UZ, VN, YU, | | | |
| | ZA, ZW | | | | | | |
| | RW: GH, GM, KE, | LS, MW, MZ, SD, | SL, SZ, TZ, UG, ZW, AT | , BE, CH, CY, | | | |
| | DE, DK, ES, | FI, FR, GB, GR, | IE, IT, LU, MC, NL, PT | , SE, TR, BF, | | | |
| | BJ, CF, CG, | CI, CM, GA, GN, | GW, ML, MR, NE, SN, TD | , TG | | | |
| | | | US 1999-167035P | P 19991123 | | | |
| | CA 2391952 | A1 20010531 | CA 2000-2391952 | 20001122 | | | |
| | | | US 1999-167035P | | | | |
| | | | WO 2000-IB1881 | | | | |
| | | | EP 2000-981535 | | | | |
| | R: AT, BE, CH, | DE, DK, ES, FR, | GB, GR, IT, LI, LU, NL | , SE, MC, PT, | | | |
| | IE, SI, LT, | LV, FI, RO, MK, | | | | | |
| | | | | P 19991123 | | | |
| | HG CE 41 CC1 | 71 00000101 | WO 2000-IB1881 | | | | |
| | US 6541661 | B1 20030401 | US 2000-718265 | 20001122 | | | |
| | JP 2003514904 | ш 00000400 | US 1999-167035P | | | | |
| | JP 2003314904 | T 20030422 | JP 2001-540085 | 20001122 | | | |
| | | | US 1999-167035P | | | | |
| | AU 783504 | B2 20051103 | | W 20001122 | | | |
| | A0 703304 | BZ 20031103 | US 1999-167035P | 20001122 | | | |
| | | | WO 2000-IB1881 | | | | |
| | EP 1748046 | A2 20070131 | EP 2006-11600 | | | | |
| | | | FI, FR, GB, GR, IE, IT, | | | | |
| | NI. PT. SE. | TR, AL, LT, LV, | MK DO ST | , LI, LU, MC, | | | |
| | , 11, 52, | 111, 122, 21, 20, | US 1999-167035P | P 19991123 | | | |
| | | | EP 2000÷981535 | | | | |
| | AU 2006200456 | A1 20060302 | AU 2006-200456 | 20060202 | | | |
| | | 20000302 | AU 2000-200436
AU 2001-18768 | | | | |
| os | MARPAT 135:5455 | | 110 2001 10700 | 110 20001122 | | | |

GΙ

AB The title compds. Cyllary1ConHz [Cy = (un)substituted cycloalkyl, aryl, heteroaryl, etc.; L1 = (CH2)mW (wherein m = 0-4; W = CONH, SO2NH, NHCO, NHSO2, NHCONH); Ar = (un)substituted arylene which may be fused to an aryl, heteroaryl, etc.; Y1 = a bond, alkylene; Z = anilinyl, pyridyl, thiadiazolyl, OM (M = H, a pharmaceutically acceptable cation)], useful for inhibiting histone deacetylase enzymic activity, were prepared E.g., a multi-step synthesis of the title compound I which showed IC50 of 7 μM against histone deacetylase in nuclear exts. from H446 cells (pooled HDACs), was given. The invention also provides compns. and methods for treating cell proliferative diseases and conditions.

Ι

RE.CNT 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN

TI Preparation of sulfonamidobenzenehydroxamates and analogs as matrix

4 1 B 4

metalloproteinase and TACE inhibitors

- AN 1999:495123 CAPLUS
- DN 131:129760
- TI Preparation of sulfonamidobenzenehydroxamates and analogs as matrix metalloproteinase and TACE inhibitors
- IN Levin, Jeremy Ian; Du, Mila T.; Venkatesan, Aranapakam Mudumbai; Nelson, Frances Christy; Zask, Arie; Gu, Yansong
- PA American Cyanamid Co., USA
- SO U.S., 68 pp. CODEN: USXXAM
- DT Patent
- LA English
- FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----|------------|------|----------|------------------|----------|
| | | | | | |
| ΡI | US 5929097 | Α | 19990727 | US 1997-944593 | 19971006 |
| | | | | US 1996-28504P P | 19961016 |

- OS MARPAT 131:129760
- AB RSO2N(CH2R7)ZCONHOH [I; R = (un)substituted (hetero)aryl; R7 = H, alkyl, Ph, etc.; Z = (un)substituted phenylene or -naphthylene] were prepared Thus, 2-(H2N)C6H4CO2Me was amidated by 4-(MeO)C6H4SO2Cl and the N-benzylated product converted in 2 steps to I [R = C6H4(OMe)-4, R7 = Ph, Z = 1,2-phenylene]. Data for biol. activity of I were given.
- RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT
- L11 ANSWER 7 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN
- TI The preparation and use of ortho-sulfonamido aryl hydroxamic acids as matrix metalloproteinase and TACE inhibitors
- AN 1998:251153 CAPLUS
- DN 128:308308
- TI The preparation and use of ortho-sulfonamido aryl hydroxamic acids as matrix metalloproteinase and TACE inhibitors
- IN Levin, Jeremy Ian; Du Mila, T.; Venkatesan, Aranapakam Mudumbai; Nelson, Frances Christy; Zask, Arie; Gu, Yansong
- PA American Cyanamid Company, USA
- SO PCT Int. Appl., 164 pp. CODEN: PIXXD2
- DT Patent
- LA English
- FAN.CNT 1

| | PATENT NO. | | | KIND DATE | | | APPLICATION NO. | | | | DATE | | | | | | | |
|----|------------|------|-----|-----------|-----|-----|-----------------|-------|------|-----|------|--------|------------|-----|------|------|--------------|------|
| ΡI | WO | 9816 | 503 | | | A2 | | 1998 | 0423 | Ţ | NO : | 1997-1 | - - | 280 | | 1 | - - | 008 |
| | | W: | AL, | AM, | ΑT, | AU, | ΑZ, | BA, | BB, | BG, | BR | , BY, | CA, | CH. | CN. | CU. | CZ. | DE. |
| | | | DK, | EE, | ES, | FI, | GB, | GE, | GH, | HU, | IL | , IS, | JP, | KE. | KG. | KP. | KR. | KZ. |
| | | | LC, | LK, | LR, | LS, | LT, | LU, | LV, | MD, | MG | , MK, | MN. | MW. | MX. | NO. | NZ. | PT. |
| | | | PT, | RO, | RU, | SD, | SE, | SG. | SI. | SK. | SL | , TJ, | TM. | TR. | ΤΤΤ. | IIA. | UG. | 117 |
| | | | | YU, | | - | - | • | • | • | | ,, | , | , | , | ·, | 00, | 02, |
| | | RW: | GH, | KE, | LS, | MW, | SD, | SZ, | UG, | ZW. | AT. | , BE, | CH. | DE. | DK. | ES. | TT. | FR |
| | | | GB, | GR, | IE, | IT, | LU, | MC, | NL. | PT. | SE | BF, | BJ. | CF. | CG. | CI. | CM. | GA. |
| | | | GN, | ML, | MR, | NE, | SN, | TD, | TG | • | | | , | , | ••, | U-, | 011 , | 011, |
| | | | | | | | | | | ι | JS : | 1996–1 | 73263 | 31 | | A 1 | 9961 | 016 |
| | CA | 2268 | 894 | | | A1 | | 1998 | 0423 | | | 1997-2 | | | | | 9971 | |
| | | | | | | | | | | | | 1996–1 | | | | | 9961 | |
| | | | | | | | | | | | | 1997–เ | | | | | | |
| | AU | 9851 | 458 | | | Α | | 1998 | 0511 | | | 1998-5 | | | | | 9971 | |
| | AU | 7317 | 37 | | | B2 | | 2001 | 0405 | | | | | | | - | | |
| | | | | | | | | | | τ | JS 3 | 1996-1 | 73263 | 31 | | A 1 | 9961 | 016 |
| | | | | | | | | | | | | 1997–ւ | | | | | | |
| • | EP | 9384 | 71 | | | A1 | | 19990 | 0901 | | | 1997- | | | | | 99710 | |
| | EP | 9384 | 71 | | | B1 | | 20013 | 1212 | | | | | | | - | / 1 (| |
| | | R: | AT, | BE, | CH, | DE, | DK, | ES, | FR, | GB, | GR, | IT, | LI, | LU, | NL, | SE, | PT, | IE, |

| | | | US 1996-732631 | Α | 19961016 |
|-------------------|------------|----------|-----------------|---|----------|
| | | | WO 1997-US18280 | W | 19971008 |
| BR 9712525 | Α | 19991019 | BR 1997-12525 | | 19971008 |
| | | | US 1996-732631 | Α | 19961016 |
| | | | WO 1997-US18280 | W | 19971008 |
| CN 1240429 | Α | 20000105 | CN 1997-180613 | | 19971008 |
| | | | US 1996-732631 | Α | 19961016 |
| • | | | WO 1997-US18280 | W | 19971008 |
| HU 200000641 | A2 | 20001028 | HU 2000-641 | | 19971008 |
| | | | US 1996-732631 | Α | 19961016 |
| | | | WO 1997-US18280 | W | 19971008 |
| JP 2001504809 | T | 20010410 | JP 1998-518448 | | 19971008 |
| | | | US 1996-732631 | Α | 19961016 |
| | | | WO 1997-US18280 | W | 19971008 |
| AT 210637 | T | 20011215 | AT 1997-946246 | | 19971008 |
| | | | US 1996-732631 | Α | 19961016 |
| | | | WO 1997-US18280 | W | 19971008 |
| ES 2166102 | Т3 | 20020401 | ES 1997-946246 | | 19971008 |
| | | | US 1996-732631 | Α | 19961016 |
| PT 938471 | ${f T}$ | 20020531 | PT 1997-946246 | | 19971008 |
| | | | US 1996-732631 | Α | 19961016 |
| ZA 9709233 | Α | 19990415 | ZA 1997-9233 | | 19971015 |
| | | | US 1996-732631 | Α | 19961016 |
| TW 410220 | В | 20001101 | TW 1997-8611418 | 7 | 19971015 |
| | | | US 1996-732631 | Α | 19961016 |
| KR 2000049196 | Α | 20000725 | KR 1999-703294 | | 19990415 |
| 1001150 | | | US 1996-732631 | Α | 19961016 |
| HK 1021178 | A 1 | 20020404 | HK 2000-100090 | | 20000106 |
| | | | US 1996-732631 | A | 19961016 |
| MADDAM 100 200200 | | • | WO 1997-US18280 | W | 19971008 |

OS MARPAT 128:308308 GI

AB The invention relates to novel, low mol. weight, non-peptide inhibitors of matrix metalloproteinases (e.g. gelatinases, stromelysins and collagenases) and TNF-α converting enzyme (TACE, tumor necrosis factor-α converting enzyme). The compds. are useful for the treatment of diseases in which these enzymes are implicated such as arthritis, tumor growth and metastasis, angiogenesis, tissue ulceration, abnormal wound healing, periodontal disease, bone disease, proteinuria, aneurysmal aortic disease, degenerative cartilage loss following traumatic joint injury, demyelinating diseases of the nervous system, graft rejection, cachexia, anorexia, inflammation, fever, insulin resistance, septic shock, congestive heart failure, inflammatory disease of the central nervous system, inflammatory bowel disease, HIV infection, age related macular degeneration, diabetic retinopathy, proliferative vitreoretinopathy, retinopathy of prematurity, ocular inflammation,

ΙΙ

keratoconus, Sjogren's syndrome, myopia, ocular tumors, and ocular angiogenesis/neovascularization. The invention compds. are represented by the formula ZSO2N(CH2R7)ACONHOH [I; A = (un)substituted Ph or naphthyl; Z = (un) substituted aryl, heteroaryl, or benzo-fused heteroaryl; $R7 = \bar{H}$, (un) substituted alk(en/yn)yl, Ph, naphthyl, 5- or 6-membered heteroaryl, cycloalkyl, or cycloheteroalkyl; or R7CH2NA forms a non-aromatic 1,2-benzo-fused 7- to 10-membered heterocyclic ring with an optional addition benzo fusion; where the hydroxamic acid moiety and the sulfonamido moiety are bonded to adjacent carbons on group A], and include pharmaceutically acceptable salts, optical isomers, and diastereomers. Prepns. of over 400 compds., including I and their intermediates, are given. For instance, 2-[(4-methoxybenzenesulfonyl)amino]-3-methylbenzoic acid Me ester (preparation given) was N-alkylated by 3-picolyl chloride-HCl (83%), followed by hydrolysis of the ester with LiOH in aqueous THF (100%), activation with oxalyl chloride, and hydroxamidation with NH2OH.HCl (51%), to give title compound II. At 50 mg/kg/day in rats with cartilage implants, II gave 44.6% inhibition of cartilage weight loss, and 51.2% inhibition of cartilage collagen loss.

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Connecting via Winsock to STN

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LOGINID: SSSPTA1623PAZ

PASSWORD:

* * * * * RECONNECTED TO STN INTERNATIONAL * * * * * * * SESSION RESUMED IN FILE 'CAPLUS' AT 12:56:05 ON 20 FEB 2007 FILE 'CAPLUS' ENTERED AT 12:56:05 ON 20 FEB 2007 COPYRIGHT (C) 2007 AMERICAN CHEMICAL SOCIETY (ACS)

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FILE 'REGISTRY' ENTERED AT 10:20:20 ON 20 FEB 2007

L1 STRUCTURE UPLOADED L2 2 SEARCH L1 EXACT FULL

L3 0 \\D SCAN

FILE 'CAPLUS' ENTERED AT 10:40:19 ON 20 FEB 2007 2 L2

FILE 'REGISTRY' ENTERED AT 11:23:51 ON 20 FEB 2007

L5 STRUCTURE UPLOADED

L6 0 SEARCH L5 SSS SAM

L7 29 SEARCH L5 SSS FULL SAVE TEMP L7 RAWHITS/A

FILE 'CAPLUS' ENTERED AT 11:26:30 ON 20 FEB 2007

L8 12 L7

SAVE TEMP L8 1STSTABHITS/A ENDS/A SAVE TEMP L8 ONESTABHITS/A

FILE 'REGISTRY' ENTERED AT 11:57:25 ON 20 FEB 2007

L9 STRUCTURE UPLOADED

L10 5 SEARCH L9 SSS SAM

FILE 'CAPLUS' ENTERED AT 11:59:30 ON 20 FEB 2007 L11 7 L10

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L4

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http://www.cas.org/ONLINE/UG/regprops.html

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AND TECHNOLOGY CORPORATION, AND FACHINFORMATIONSZENTRUM KARLSRUHE

FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Feb 16, 2007 (20070216/UP).

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COST IN U.S. DOLLARS SINCE FILE TOTAL

FULL ESTIMATED COST ENTRY SESSION 0.06 349.89

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE TOTAL ENTRY SESSION

CA SUBSCRIBER PRICE ENTRY SESSION 0.00 -16.38

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STRUCTURE FILE UPDATES: 19 FEB 2007 HIGHEST RN 921921-74-6 DICTIONARY FILE UPDATES: 19 FEB 2007 HIGHEST RN 921921-74-6

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TSCA INFORMATION NOW CURRENT THROUGH June 30, 2006

Please note that search-term pricing does apply when conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

=> search 19 sss full FULL SEARCH INITIATED 12:59:08 FILE 'REGISTRY' FULL SCREEN SEARCH COMPLETED - 100701 TO ITERATE

100.0% PROCESSED 100701 ITERATIONS 318 ANSWERS SEARCH TIME: 00.00.02

L12 318 SEA SSS FUL L9

=> d scan

L12 318 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN

IN 2-Propenamide, 3-[4-[[(9-ethyl-9H-carbazol-3-yl)amino]sulfonyl]phenyl]-N-hydroxy-, (2E)- (9CI)

MF C23 H21 N3 O4 S

Double bond geometry as shown.

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):6

L12 318 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN

MF C16 H16 N2 O5 S

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L12 318 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN IN Benzamide, N-hydroxy-2-[[(4-methoxyphenyl)amino]sulfonyl]- (9CI)

MF C14 H14 N2 O5 S

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L12 318 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN

IN Benzamide, 4-[[[4-[(hydroxyamino)carbonyl]phenyl]amino]sulfonyl]-N,Ndimethyl- (9CI)

MF C16 H17 N3 O5 S

L12 318 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN

IN 2-Propenamide, N-hydroxy-3-[4-[(2-naphthalenylamino)sulfonyl]phenyl](9CI)

MF C19 H16 N2 O4 S

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L12 318 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN

IN 2-Propenamide, N-hydroxy-3-[4-[[(4-nitrophenyl)sulfonyl]amino]phenyl](9CI)

MF C15 H13 N3 O6 S

$$\begin{array}{c|c}
O_2N & O_1 & O_2N \\
O_3 & O_4 & O_5 & O_6
\end{array}$$

$$\begin{array}{c|c}
CH = CH - C - NH - OH \\
O_4 & O_6
\end{array}$$

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L12 318 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN

IN Benzamide, 4-[[[2-(diethylamino)-6-quinolinyl]sulfonyl]amino]-N-hydroxy-,
mono(trifluoroacetate) (salt) (9CI)

MF C20 H22 N4 O4 S . C2 H F3 O2

CM 1

CM 2

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):20

L12 318 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN

MF C13 H12 N2 O4 S2

Double bond geometry as shown.

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L12 318 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN

MF C16 H16 N2 O4 S

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L12 318 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN IN Benzamide, 4-[[[2-[(3,4-difluorophenyl)methyl]-6-benzoxazolyl]sulfonyl]amino]-N-hydroxy- (9CI) MF C21 H15 F2 N3 O5 S

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L12 318 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN
IN 2-Propenamide, 3-[3-[[[3,5-bis(trifluoromethyl)phenyl]amino]sulfonyl]pheny
l]-N-hydroxy-, (2E)- (9CI)
MF C17 H12 F6 N2 O4 S

Double bond geometry as shown.

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L12 318 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN
IN 2-Propenamide, 3,3-bis[3-[[(4-bromophenyl)sulfonyl]amino]phenyl]-N-hydroxy(9CI)
MF C27 H21 Br2 N3 O6 S2

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

318 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN

2-Heptene-4,6-diynamide, N-hydroxy-7-[3-[(phenylsulfonyl)amino]phenyl]-, IN (E)-(9CI)

C19 H14 N2 O4 S MF

Double bond geometry as shown.

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L12 318 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN

Benzamide, 4-[[[4-(dimethylamino)phenyl]sulfonyl]amino]-N-hydroxy- (9CI) IN

MF C15 H17 N3 O4 S

CI COM

$$\begin{array}{c|c} O & O \\ \parallel & C-NH-OH \\ \hline S-NH & O \\ O & O \end{array}$$

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

REGISTRY COPYRIGHT 2007 ACS on STN L12 318 ANSWERS

2-Propenamide, 3-[3-[[[4-(difluoromethoxy)phenyl]amino]sulfonyl]phenyl]-Nhydroxy- (9CI) C16 H14 F2 N2 O5 S

MF

L12 318 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN
IN Benzamide, 4-[(benzo[b]thien-2-ylsulfonyl)amino]-N-hydroxy- (9CI)
MF C15 H12 N2 O4 S2

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L12 318 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN

IN Benzamide, 4-[[(3,5-dimethyl-4-isoxazolyl)sulfonyl]amino]-N-hydroxy- (9CI)

MF C12 H13 N3 O5 S

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L12 318 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN

IN 2-Propenamide, N-hydroxy-3-[4-[[(4-methoxyphenyl)sulfonyl]amino]phenyl]-,
(2E)- (9CI)

MF C16 H16 N2 O5 S

Double bond geometry as shown.

L12 318 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN

IN 2-Propenamide, 3-[4-[(2-dibenzofuranylsulfonyl)amino]phenyl]-N-hydroxy(9CI)

MF C21 H16 N2 O5 S

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L12 318 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN

IN 3-Thiophenecarboxylic acid, 5-[[[4-[(hydroxyamino)carbonyl]phenyl]amino]su
lfonyl]-4-methoxy-, methyl ester (9CI)

MF C14 H14 N2 O7 S2

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L12 318 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN

Double bond geometry as shown.

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L12 318 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN

IN 2-Propenamide, N-hydroxy-3-phenyl-3-[3-[[[4-(trifluoromethyl)phenyl]sulfon yl]amino]phenyl]-, (2Z)- (9CI)

MF C22 H17 F3 N2 O4 S

Double bond geometry as shown.

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L12 318 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN

IN Benzamide, 4-[[(5-chloro-3-methylbenzo[b]thien-2-yl)sulfonyl]amino]-N-hydroxy- (9CI)

MF C16 H13 C1 N2 O4 S2

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L12 318 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN

IN 2-Propenamide, N-hydroxy-3-[2-[(2-naphthalenylamino)sulfonyl]phenyl]-,

(2E) - (9CI) MF C19 H16 N2 O4 S

Double bond geometry as shown.

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L12 318 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN

IN 2-Propenamide, N-hydroxy-3-[2-[[(4-methoxyphenyl)sulfonyl]amino]-5-nitrophenyl]-3-phenyl-, (2E)- (9CI)

MF C22 H19 N3 O7 S

Double bond geometry as shown.

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

'L12 318 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN

MF C24 H28 N2 O4 S

L12 318 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN
IN Benzamide, N-hydroxy-4-[[[4-(1-methylethyl)phenyl]sulfonyl]amino]- (9CI)
MF C16 H18 N2 O4 S

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

=> save temp 112 rawsulphamde/a
ANSWER SET L12 HAS BEEN SAVED AS 'RAWSULPHAMDE/A'

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=> 112

L13 131 L12

=> file save temp 113 sulphnmderefs/a
'SAVE' IS NOT A VALID FILE NAME
Enter "HELP FILE NAMES" at an arrow prompt (=>) for a list of files
that are available. If you have requested multiple files, you can
specify a corrected file name or you can enter "IGNORE" to continue
accessing the remaining file names entered.
ENTER A FILE NAME OR (IGNORE):end

=> save temp 113 sulphnmderefs/a SULPHNMDEREFS/A IS NOT A VALID SAVED NAME Enter the name you wish to use for the saved query, answer set, or L-number list. The name must:

- 1. Begin with a letter,
- 2. Have 1-12 characters,
- 3. Contain only letters (A-Z) and numbers (0-9),
- End with /Q for a query (search profile, structure, or screen set), /A for an answer set, or /L for an L-number list.
- 5. Not already be in use as a saved name,
- 6. Not be END, SAV, SAVE, SAVED
- 7. Not have the form of an L-number (Lnnn). ENTER NAME OR (END):end

=> save temp 113 sulphrefs/a
ANSWER SET L13 HAS BEEN SAVED AS 'SULPHREFS/A'

=> d 113 125-131 ti

- L13 ANSWER 125 OF 131 CAPLUS COPYRIGHT 2007 ACS on STN
- TI Silver halide photographic material containing hydrazine compound
- L13 ANSWER 126 OF 131 CAPLUS COPYRIGHT 2007 ACS on STN
- TI Preparation of aromatic hydroxamic acid compounds for preventing and treating neurodegenerative diseases
- L13 ANSWER 127 OF 131 CAPLUS COPYRIGHT 2007 ACS on STN
- TI Oxamflatin: a novel compound which reverses malignant phenotype to normal one via induction of JunD
- L13 ANSWER 128 OF 131 CAPLUS COPYRIGHT 2007 ACS on STN
- TI (2E)-5-[3-[(Phenylsulfonyl)amino]phenyl]- pent-2-en-4-ynohydroxamic Acid and Its Derivatives as Novel and Potent Inhibitors of ras Transformation
- L13 ANSWER 129 OF 131 CAPLUS COPYRIGHT 2007 ACS on STN

- TI Preparation of sulfonamidoaryl hydroxamic acids as inflammation and tumor inhibitors
- L13 ANSWER 130 OF 131 CAPLUS COPYRIGHT 2007 ACS on STN
- TI Synthesis and screening of some new methyl salicylate-5-sulfonamides containing active units as analgesic agents
- L13 ANSWER 131 OF 131 CAPLUS COPYRIGHT 2007 ACS on STN
- TI o-Hydroxybenzohydroxamic acids
- => d 113 126-131 ti fbib abs
- L13 ANSWER 126 OF 131 CAPLUS COPYRIGHT 2007 ACS on STN
- TI Preparation of aromatic hydroxamic acid compounds for preventing and treating neurodegenerative diseases
- AN 1996:733885 CAPLUS
- DN 126:7829
- TI Preparation of aromatic hydroxamic acid compounds for preventing and treating neurodegenerative diseases
- IN Kato, Kaneyoshi; Miki, Shokyo; Naruo, Ken-Ichi; Takahashi, Hideki
- PA Takeda Chemical Industries, Ltd., Japan
- SO Eur. Pat. Appl., 83 pp. CODEN: EPXXDW
- DT Patent
- LA English
- FAN.CNT 1

| | PA' | PATENT NO. | | | KIND | | DATE | | APPLICATION NO. | | | DATE | | | | | |
|----|-------------------------------------|------------|-----|-----|----------------|-----|----------------------------------|------|-----------------|------------|-------|------------|----------|------|------|-----|----|
| PI | EP 737671
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EP 737671 | | | | A2
A3
B1 | | 19961016
19970502
20011212 | | EP 1996-302494 | | | 19960410 | | | | | |
| | | R: AT, | BE, | CH, | DE, | DK, | ES, | FI, | FR, G | | | | | | | | SE |
| | | | | | | | | | | 1995 | | | | | 9950 | | |
| | | | | | | | | | JP 1995-215932 | | | A 19950824 | | | | | |
| | JP | 09118660 | | | Α | | 1997 | 0506 | JP | 1996-86160 | | 19960409 | | | | | |
| | | | | | | | | | JP | 1995 | -8434 | 12 | P | 1 | 9950 | 410 | |
| | | | | | | | | | JP | 1995 | -2159 | 32 | P | 1 | 9950 | 824 | |
| | US | 5804601 | | | Α | | 19980908 | | US 1996-629623 | | | 19960409 | | | | | |
| | | | | | | | | | JP | 1995 | -8434 | 12 | P | 1 | 9950 | 410 | |
| | | | | | | | | | JP | 1995 | -2159 | 32 | P | 1 | 9950 | 824 | |
| | CA | 2173806 | | | A1 | | 1996 | 1011 | CA | 1996 | -2173 | 806 | | 1 | 9960 | 410 | |
| | | | | | | | | | JP | 1995 | -8434 | 12 | A | 1 | 9950 | 410 | |
| | | | | | | | | | JP | 1995 | -2159 | 32 | A | . 1 | 9950 | 824 | |
| | ни 9600924 | | | | A 2 | | 19970128 | | HU 1996-924 | | | | 1 | 9960 | 410 | | |
| | | | | | | | | | | 1995-84342 | | / A | . 1 | 9950 | 410 | | |
| | | | | | | | | | JP | 1995 | -2159 | 32 | A | 1 | 9950 | 824 | |
| | ΑT | 210635 | • | | T | | 2001 | 1215 | | 1996 | | | • | | 9960 | | |
| | | | | | | | | | | 1995 | | | Δ. | | 9950 | | |
| | | | | | | | | | | 1995 | | | | | 9950 | | |
| ~~ | | DD 106 | | | | | | | OL | 1000 | 210 | | - | . т | 2230 | 024 | |

- OS MARPAT 126:7829
- The title compds. ArR1CHCH2QCONHOR2 (I) and ArR1C:CHQCONHOR2 [II; R1 = H, cyano, an optionally substituted hydrocarbon or Ph or naphthyl, NR3R4, acyl; R2 = acyl; R3, R4 = H, acyl, optionally substituted hydrocarbon group, or R3 and R4 may combine together with the adjacent N atom to form a ring; Ar = (un)substituted C6-14 aryl or 5-11 membered heteroaryl; Q = divalent C2-8 aliphatic hydrocarbon group] or salts thereof are prepared I and II (R2 = H, acyl) having excellent anti-neurodegenerative activity with a low cytotoxicity are useful for preventing or treating neurodegenerative diseases such as Alzheimer's disease, Parkinson's disease, Down's syndrome, Pick's disease, multiple sclerosis, and diseases typically mediated by viral infections, etc. Thus, 6-(4-methoxyphenyl)-6-(3-methyl-1,4-naphthoquinon-2-yl)hexanohydroxamic acid was reacted with Ac20 in the

presence of pyridine to give I (R1 = 3-methyl-1,4-naphthoquinon-2-yl, Ar = 4-MePh, Q = (CH2)3, R2 = Ac). I (R1 = 3-methyl-1,4-naphthoquinon-2-yl, Ar = 4-MeOPh, Q = (CH2)3, R2 = H) showed IC50 of 0.08 μ M against lipopolysaccharides-induced NO production in a mixed rat cerebral cell culture system.

- L13 ANSWER 127 OF 131 CAPLUS COPYRIGHT 2007 ACS on STN
- TI Oxamflatin: a novel compound which reverses malignant phenotype to normal one via induction of JunD
- AN 1996:463426 CAPLUS
- DN 125:157903
- TI Oxamflatin: a novel compound which reverses malignant phenotype to normal one via induction of JunD
- AU Sunoda, Hikaru; Nishida, Kazuyo; Takayuki, Nishida; Yoshioka, Takayuki; Ohtani, Mitsuaki; Sugita, Kenji
- CS Shionogi Res. Lab., Shionogi & Co., Ltd., Osaka, 553, Japan
- SO Oncogene (1996), 13(1), 143-149 CODEN: ONCNES; ISSN: 0950-9232
- PB Stockton
- DT Journal
- LA English
- AB In the course of screening for inhibitors of tumorigenic phenotype of K-ras-transformed NIH3T3 cells (DT cells), we found a novel compound, oxamflatin, an aromatic sulfonamide hydroxamate derivative, which induces flat phenotype in these cells and suppresses their anchorage-independent growth. In contrast to dT cells, in v-raf-transformed NIH3T3 cells, no change in their morphol. and no specific inhibition of their anchorage-independent growth was observed Interestingly, oxamflatin was effective to NIH3T3 cells transformed by constitutively activated mutant of MEK, indicating the possibility that oncogene-induced morphol. change is not necessarily induced by common signaling pathway such as MAP kinase cascade. In oxamflatin-treated DT cells, the expression of transcription factor junD was highly augmented, resulting in trans-activation of fibronectin gene by junD via cAMP responsive element in its promoter. This behavior of junD was confirmed to correlate well with partial blocking of malignant phenotype in DT cells. Thus, oxamflatin can be categorized as the first reagent which induces genes whose products can interfere with oncogene-dependent transformation.
- .L13 ANSWER 128 OF 131 CAPLUS COPYRIGHT 2007 ACS on STN
- TI (2E)-5-[3-[(Phenylsulfonyl)amino]phenyl]- pent-2-en-4-ynohydroxamic Acid and Its Derivatives as Novel and Potent Inhibitors of ras Transformation
- AN 1996:382877 CAPLUS
- DN 125:75336
- TI (2E)-5-[3-[(Phenylsulfonyl)amino]phenyl]- pent-2-en-4-ynohydroxamic Acid and Its Derivatives as Novel and Potent Inhibitors of ras Transformation
- AU Ohtani, Mitsuaki; Matsuura, Takaharu; Shirahase, Kazuhiro; Sugita, Kenji
- CS Shionogi Research Laboratories, Shionogi Co., Osaka, 553, Japan
- SO Journal of Medicinal Chemistry (1996), 39(15), 2871-2873 CODEN: JMCMAR; ISSN: 0022-2623
- PB American Chemical Society
- DT Journal
- LA English
- OS CASREACT 125:75336
- AB In the course of screening compds. exhibiting reversion of the cell morphol. transformed by ras-oncogene, the authors found a novel type of aromatic hydroxamic acid derivs. Structure-activity relation (SAR) study was tried and (2E)-5-[3-(phenylsulfonylamino)phenyl]pent-2-en-4-ynohydroxamic acid was found to show very potent activity with an MIC value of 0.04 µM. It reversed the phenotype of ras-transformed cells to the normal one, indicating reversion of tumor characteristic to normal one. This is the first report describing the synthesis of novel aromatic conjugated hydroxamic acid derivs. inducing genes with products that can interfere

- L13 ANSWER 129 OF 131 CAPLUS COPYRIGHT 2007 ACS on STN
- TI Preparation of sulfonamidoaryl hydroxamic acids as inflammation and tumor inhibitors
- AN 1994:54333 CAPLUS
- DN 120:54333
- TI Preparation of sulfonamidoaryl hydroxamic acids as inflammation and tumor inhibitors
- IN Ohtani, Mitsuaki; Arita, Hitoshi; Sugita, Kenji; Matsuura, Takaharu; Shirahase, Kazuhiro
- PA Shionogi and Co., Ltd., Japan
- SO PCT Int. Appl., 125 pp. CODEN: PIXXD2
- DT Patent
- LA Japanese

FAN.CNT 1

| | PA | rent i | NO. | | | KIND

A1 | | DATE

19930624 | | | | | | | | DATE

19921207 | | |
|----|-------|------------|------------|-----------|----------|----------------|----------------|----------------------|------|----------------|-------------------------|------|----|---|------|-------------------------|------|--|
| PI | WO | 9312
W: | 075
JP, | | | | | | | | | | | | | | | |
| | | RW: | AT, | BE, | CH, | DE, | DK, | ES, | FR, | GB, G | R, IE,
1991- | | | | | | | |
| | ΕP | 5705 | A1 | | 19931124 | | EP 1992-924883 | | | | | | | | | | | |
| | ΕP | | | | | | | 19970730 | | | | | | | _ | | .201 | |
| | | R: | AT, | BE, | CH, | DE, | DK, | ES, | FR, | | 1991- | 3507 | 93 | | A 1 | 9911 | 210 | |
| | АТ | 1561 | 16 | | | T | | 1997 | 0815 | AT | 1992-
1992-
1991- | 9248 | 83 | | 1 | .9921
.9921
.9911 | 207 | |
| | ES | 2107 | 557 | | | Т3 | | 1997 | 1201 | ES | 1992-
1991- | 9248 | 83 | | 1 | .9911
.9921
.9911 | 207 | |
| | JР | JP 3342485 | | | В2 | | 20021111 | | JP | 1993-
1991- | 5107 | 75 | | 1 | 9921 | 207 | | |
| | *** | 5504 | c | | | | | | | WO | 1992- | JP15 | 93 | | _ | .9911
.9921 | | |
| | บร | 55346 | 054 | | | A | | 19960 | 0709 | | 1993-
1991- | | | i | | .9930
.9911 | | |
| 00 | C 3 C | ים ביותי | . 10/ | 5 . E 4 : | | 163.55 | | 100 | | | 1992- | JP15 | 93 | Ţ | W 1 | 9921 | 207 | |

Q=
$$XCONR^{1}OR^{2}$$
 $NHSO_{2}Ph$ III
 $C \equiv CCH = CHCONHOH$
 $NHSO_{2}Ph$ III

AB The title compds. R2ONR1COXA1YNR3BA2 (I) [Al = (substituted) aromatic ring, aromatic heterocyclic ring; A2 = H, (substituted) aryl, aromatic heterocyclic ring; B = single bond, B1B2; B1 = CO, SO2; B2 = alkylene, alkenylene, etc.; X = (substituted) alkylene which may have O, S, N and may have unsatd. bond; Y = single bond, heteroatom, (substituted) alkylene which may contain heteroatom and may have unsatd. bond; X and N (which is linked to Y) may together form a moiety Q; R1 - R3 = H, (substituted) alkyl,

aryl] were prepared I inhibit hemangioendothelial cell growth, the development of a lymphocyte adhesion factor, and ras gene-induced cell transformation and are useful as inflammation and tumor inhibitors. Condensation of carboxylic acid (E)-II (R = OH) with NH2OH.HCl in DMF containing N-hydroxysuccinimide, N,N-dicyclohexylcarbodiimide, and Et3n gave (E)-II (R = NHOH). Hydroxamic acid (E)-III in vitro exhibited MIC of 0.039 μ M against ras gene-induced cell transformation.

L13 ANSWER 130 OF 131 CAPLUS COPYRIGHT 2007 ACS on STN

TI Synthesis and screening of some new methyl salicylate-5-sulfonamides containing active units as analgesic agents

AN 1989:614401 CAPLUS

DN 111:214401

TI Synthesis and screening of some new methyl salicylate-5-sulfonamides containing active units as analgesic agents

AU Hannout, I. B.; Sharief, A. M. Sh.; Ammar, Y. A.; Mohamed, Y. A.; Youssef, A. A.

CS Fac. Sci., Al-Azhar Univ., Cairo, Egypt

Journal of the Serbian Chemical Society (1988), 53(7), 353-61 CODEN: JSCSEN; ISSN: 0352-5139

DT Journal

LA English

OS CASREACT 111:214401

GΙ

OH OH
$$CO_2Me$$
 CO_1R^2 CO_2Me I $SO_2NR^1R^2$ II

AB Treatment of ClSO2C6H3(CO2Me)OH-3,4 with amines under various conditions afforded sulfonamides, e.g. I (R = alkyl, aryl) or amidosulfonylsalicylamides, e.g. II (R1 = H, R2 = cyclohexyl, 4-AcC6H4). Seven products were screened for toxicity and exhibited mild or weak analgesic activity.

L13 ANSWER 131 OF 131 CAPLUS COPYRIGHT 2007 ACS on STN

TI o-Hydroxybenzohydroxamic acids

AN 1958:56242 CAPLUS

DN 52:56242

OREF 52:10184a-d

TI o-Hydroxybenzohydroxamic acids

IN Priewe, Hans; Rutkowski, Rudi

PA Schering A.-G.

DT Patent

LA Unavailable

FAN.CNT 1

PATENT NO. KIND DATE APPLICATION NO. DATE

PI DE 855866 19521117 Di

o-Hydroxybenzohydroxamic acids are obtained by the reaction of p-substituted o-hydroxybenzoic esters with NH2OH in alkaline solns. with subsequent isolation of the free acids. Examples: 167 g. Me 4-amino-2-hydroxybenzoate and 90.4 g. NH2OH.HCl (I) in 2 l. 2N NaOH left to stand for several hrs. and treated with HCl gives 4-amino-2-hydroxybenzohydroxamic acid-HCl. Treatment with bicarbonate solution gives 106 g. free acid, needles, m. 187° (decomposition). Me

4-nitro-2-hydroxybenzoate (1 mole) with 1.3 moles I gives 65%
4-nitro-2-hydroxybenzohydroxamic acid, light yellow needles, m.
214°; Me 4-acetamido-2-hydroxybenzoate (1 mole) with 1.3 moles I
gives 64.5% 4-acetamido-2-hydroxybenzohydroxamic acid, m. 218°; Me
N-carbethoxy-4-amino-2-hydroxybenzoate (f.p. 145°, 8 g.) with 7 g.
I gives 49.6% N-carbethoxy-4-amino-2-hydroxybenzohydroxamic acid, m.
178-9°; Me 3,5-dibromo-4-amino-2-hydroxybenzoate (m.
138-40°) with I gives 3,5-dibromo-4-amino-2-hydroxybenzohydroxamic acid, m. 194-5°; Me 4-iodosalicylate (1.2 g.) with 0.4 g. I gives
57% 4-iodo-2-hydroxybenzohydroxamic acid, m. 202° (decomposition); Me
4-benzenesulfonamido-2-hydroxybenzoate (2.3 g., m. 189-90°) with
0.7 g. I gives 59% 4-benzenesulfonamido-2-hydroxybenzohydroxamic acid, m.
222° (decomposition).

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